VOL. 35 TORONTO, DECEMBER, 1936 No. 6
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PUBLISHED MONTHLY BY
THE CANADIAN MEDICAL ASSOCIATION
3640 UNIVERSITY STREET, MONTREAL

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The Canadian
Medical Association Journal

Vol. 35 TORONTO, DECEMBER, 1936 No. 6

THE RADIOLOGICAL TREATMENT OF CANCER
1929 – 1935

V. CARCINOMA OF THE TONGUE*

BY G. E. RICHARDS, M.D., F.R.C.P.(C.)

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Toronto

SECOND only in importance to actual cure of the disease is conservation of tissue in the treatment of cancer of the tongue, and in this respect radiotherapy offers distinct advantages. When radiotherapy is completely successful the scarring which results is comparatively slight, and the tissues remain soft and flexible with a very moderate degree of interference with function, either of speech or deglutition. Even under the most unfavourable circumstances the dysfunction resulting from radiotherapy cannot be compared to that which follows total excision. If therefore it can be shown that the primary lesion can be controlled by radiotherapy to a reasonable degree it would appear that an important gain in treatment has been achieved. The problem of glandular secondaries on the other hand is common to both surgery and radiology and is still the great stumbling-block in the treatment of all types of oral cancer.

In the series of cases reported in the present paper the primary lesion has been treated radiologically as the primary procedure, whereas surgery, diathermy, etc., have been used as adjuncts to radiotherapy. In dealing with the glandular secondaries, on the contrary, surgery has been the primary method with radiotherapy, either external or interstitial, adjunct to it.

Material.—The present series comprises 101 cases treated during the period 1929-1935. Fifteen were females and 86 males. The ages according to decades were as follows:—

TABLE I

10–19	20–29	30–39	40–49	50–59
–	–	–	9	35
60–69	**70–79**	**80–89**	**90–99**	**not stated**
31	22	3	–	1

Classification. — The primary lesions were divided into four groups, depending upon the extent and duration of the lesion, while glandular secondaries were classified in three groups as in the other varieties of oral cancer.* Seventeen of the primary lesions were classified in Group "A"—early; 42 in Group "B"—moderately advanced; 31 in Group "C"—far advanced; and 11 in Group "D"—hopeless. Classified according to location, the lesions occupied the following sites:

TABLE II

		Male	*Female*
Tip	7	3	4
Dorsum	11	9	2
Lateral margins	54	47	7
Base	26	24	2
Not specified	3	3	–
	101	86	15

It will be noted that in respect both to extent and location the figures also express percentages and probably indicate fairly accurately the incidence of malignant involvement in the vari-

* The previous articles in this series appear in the *Journal*, 1936, **35**: 299, 381, 385, 490.

* See paper IV of this series.

ous regions of the tongue. It is interesting to note that lesions arising at the tip are more common in females than in males.

RESULTS FOR THE WHOLE GROUP

The statement of results for the whole group reflects the combined effort made both by surgical and radiological methods to control the disease as a whole, and includes all cases, both early and late, and in all regions of the tongue. From this standpoint it is found that 25 of the cases (25 per cent) are alive and symptom-free; 12 have died of extraneous diseases; 3 are alive but not free of disease; 58 have died of the disease (58 per cent); and 3 are untraced. If, however, one accepts the definition of "cure" as "disappearance of the lesion for which treatment is undertaken without recurrence during the lifetime of the patient," much interesting information is found in a study of those patients who have died of extraneous disease. The details are recorded in Table III. Three of these patients died within too short a time following treatment to provide any useful information as to the probable outcome, but in nine the above conditions were met, *viz.*, the lesion for which treatment was undertaken disappeared, healing took place without recurrence of the disease for periods of time ranging from nine months to six years, and death occurred from some other cause than cancer of the tongue. So far as these persons were concerned, their disease had been controlled. It is suggested that such a definition of "cure" is more logical than an arbitrary five-year period, especially when dealing with persons in the seventh and eighth decades of life. Considered from this point of view, the number in whom the disease was controlled is 34 of the 101 cases, *i.e.*, 34 per cent.

TABLE III

PATIENTS WHO DIED OF EXTRANEOUS DISEASE

	Age when treated	*Stage*	*Years survived*	*Cause of death*	*Recurrence*
1.	80	"B"	3 yrs.	Cardiac	No.
2.	70	"B"	1½ yrs.	Mental	No.
3.	63	"B"	1½ yrs.	Cardiac	No.
4.	58	"B"	1 mo.	Acute illness	
5.	78	"C"	5 yrs.	Pneumonia	No.
6.	70	"C"	3 wks.	Stroke	
7.	50	"B"	2 yrs.	Stroke	No.
8.	68	"C"	1 mo.	Cardiac	
9.	73	"A"	1 yr.	Erysipelas	No.
10.	61	"B"	4 mos.	Accident	
11.	55	"B"	9 mos.	Gastric hæmorrhage	No.
12.	73	"A"	6 yrs.	(Old age)	No.

Healing of the primary lesion.—As stated earlier, however, we are concerned as well with the position of radiotherapeutic measures as a means of conserving tissue in the treatment of cancer of the tongue, and are therefore interested in discovering to what extent the primary lesion was controlled even in those cases in which treatment as a whole ultimately failed. It is found that in 54 of the 101 cases (54 per cent) the primary lesion was controlled and healing took place without local recurrence during the lifetime of the individual; in 37 the primary was uncontrolled, and in 10 exact information on this point was not obtained. Undoubtedly, had all these patients lived some time longer than they actually did a certain number would have developed local recurrences, and therefore the figure is probably high, but at least indicates approximately what may be expected in this respect.

The influence of location.—In view of the generally accepted opinion that the posterior third of the tongue, due to the preponderance there of lymphoid tissue, is relatively radiosensitive, whereas the anterior third is more radio-resistant, one is interested in discovering whether satisfactory results are dependent more upon the location of the lesion upon the tongue or upon the stage of the disease at which treatment is undertaken, regardless of location. Accordingly an analysis has been made from both these aspects, and the results are shown in Tables IV and V, from which it will be seen that the stage of disease appears to be of much more importance. Table IV, showing the results according to the stage of disease, also adds its quota of emphasis to the urgent need for early diagnosis, by indicating as it does that in Group "A", or early, cases, the results of treatment are quite encouraging (59 per cent), whereas they fall off rapidly as the disease advances, and in this series all treatment was ineffective in the very late cases, regardless of location or any other consideration.

Details of results according to location on the tongue.

1. Tip: 7 cases; 4 females, 3 males. Stage A, 2; Stage B, 3; Stage C, 1; Stage D, 1. Two patients are alive and symptom-free after 3 years and 5 years; 1 died of extraneous disease after 3 years without recurrence; 4 died of the disease.

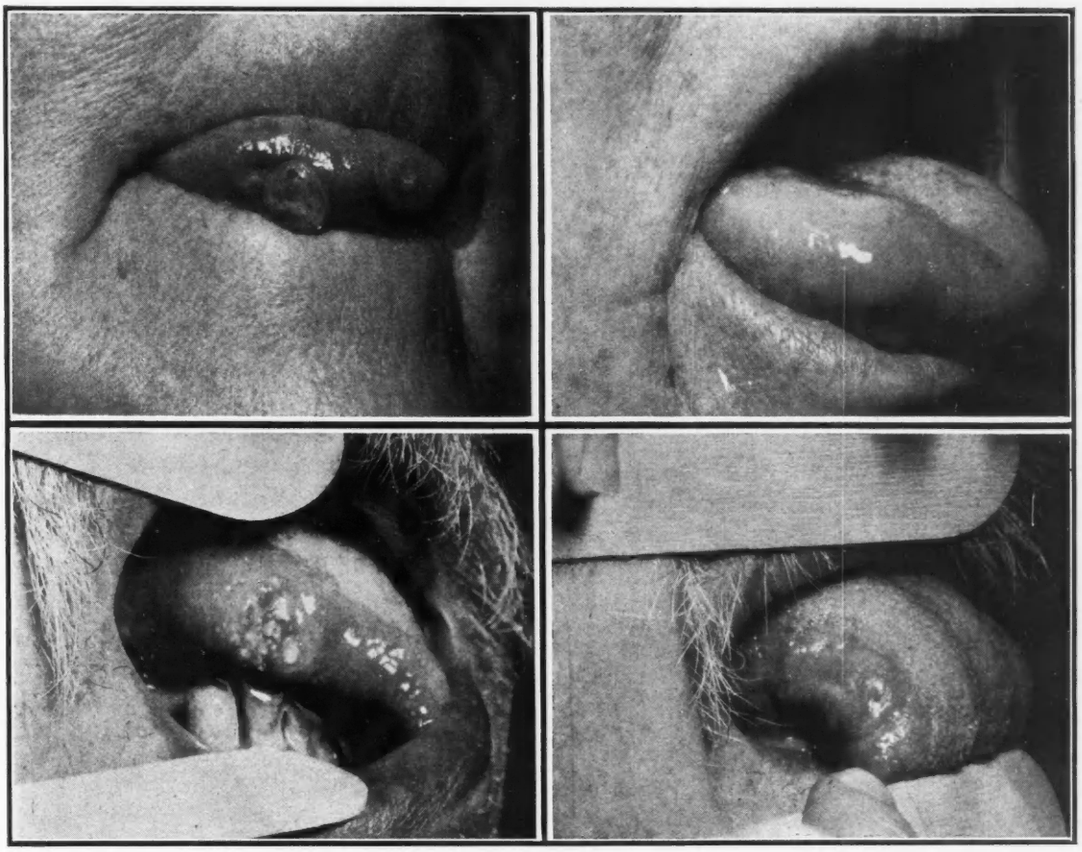

Fig. 1.—Stage I. "A"—Early. 1 to 1.5 cm. diameter; slight or no ulceration. 59.2 per cent of such lesions were controlled by treatment.

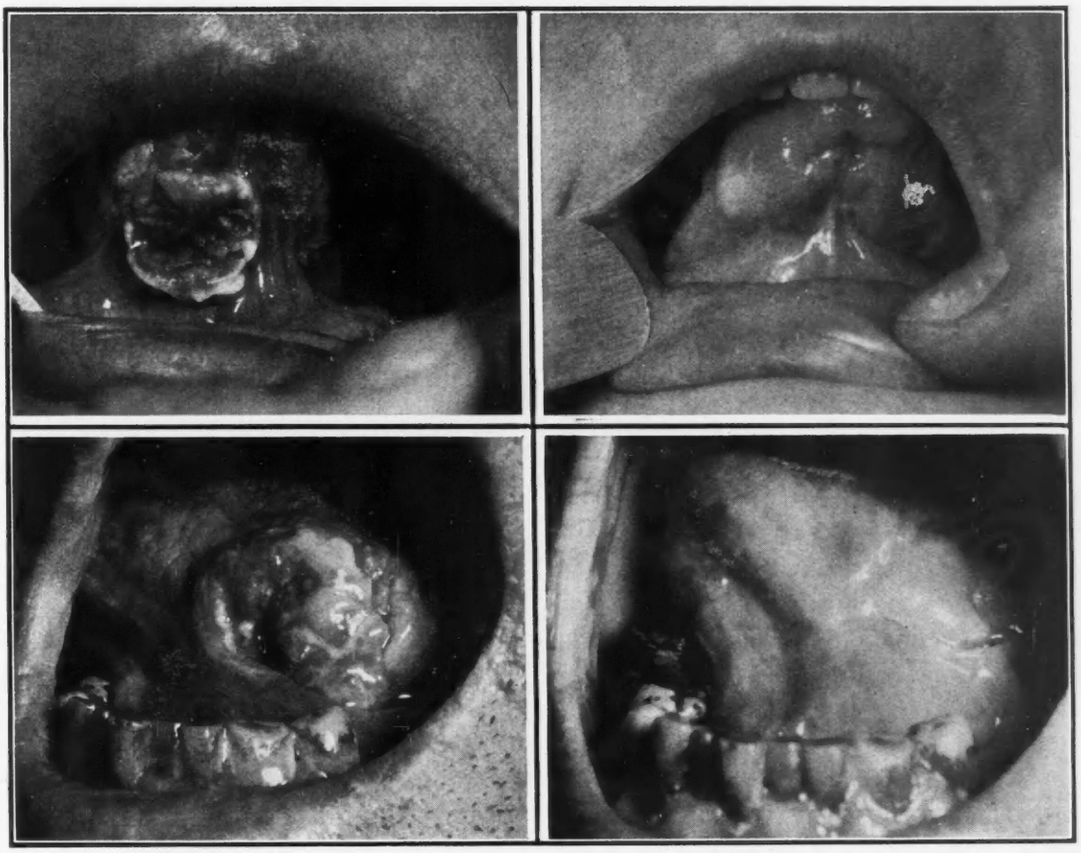

Fig. 2.—Stage II. "B"—Moderately advanced. Open ulceration; considerable infiltration. 26.1 per cent of such lesions were controlled.

TABLE IV

FOLLOW-UP ACCORDING TO STAGE OF DISEASE

Stage	*No. of patients*	*Alive and symptom-free*	*Percentage*
"A"—Early	17	9	59.2
"B"—Moderately advanced	42	11	26.1
"C"—Far advanced	31	3	10.0
"D"—Very far advanced	11	–	–

TABLE V

RESULTS ACCORDING TO LOCATION ON THE TONGUE

	No. of patients	*Alive and symptom-free*	*Percentage*
Tip	7	2	28.5
Dorsum	11	3	27.2
Lateral margins	54	12	22.2
Base	26	6	23.0

TABLE VI

FOLLOW-UP ACCORDING TO TIME SURVIVED OF PATIENTS FREE OF DISEASE AND THOSE DEAD OF EXTRANEOUS DISEASE (D.E.D.)

	Alive and well	*D.E.D.*
Under 1 year	1	5
1 to 2 years	7	3
2 to 3 years	6	1
3 to 4 years	4	1
4 to 5 years	1	–
5 to 6 years	5	1
6 to 7 years	1	1
Total	25	12

In 1 case failure was due to failure to control the primary lesion only; in 1 case was similar failure to control glandular secondaries while the primary was controlled; in 2 cases both primary and secondaries were uncontrolled.

2. Dorsum: 11 cases; 2 females, 9 males. Stage A, 1; Stage B, 1; Stage C, 5; Stage D, 4. Three patients are alive and symptom-free after 2 years and 3 years; 8 have died of the disease, in periods ranging from a few weeks to 3½ years.

Owing to the general experience that in this location malignant lesions are unusually resistant, the methods adopted have included heavy preliminary irradiation, interstitial radium in various forms, usually highly filtered needles, surgical diathermy, and total excision of the tongue (1 case). Curiously enough, two of the three successful cases showed very extensive lesions, classified as Stage "C" and thought to be almost hopeless on admission, and these were controlled by radiotherapy alone without great difficulty.

There were 8 failures in the group. Four of the cases were Stage "D", very far advanced, and in these treatment may be regarded as palliative only. In all four of these and two Stage "C" cases failure was due to extension of both the primary lesions and glandular secondaries; in one case the primary was controlled and failure was due to remote metastasis; in one case (Fig. 4) failure was due to extension of the primary lesion; no glands present.

3. Lateral margins: 54 cases; 7 females, 47 males. Stage A, 12; Stage B, 27; Stage C, 13; Stage D, 2. Healing of the primary lesion was obtained in 46.2 per cent. Twelve patients, or 22.2 per cent, are alive and symptom-free; 11 have died of various intercurrent diseases; 25, or 46 per cent, have died of the disease; 2 are untraced, and the remainder are still under treatment.

In 46.2 per cent of these cases disappearance of the primary lesion was obtained without recurrence, but owing to the abnormal percentage of deaths from intercurrent diseases this does not appear from the table as recorded above. It is our belief that lesions occurring on the lateral margins of the tongue are not only the most common but are also the most amenable to treatment, and that 46 per cent more closely approximates the cure rate than does 22 per cent.

There were 25 failures, the causes of which were as follows:

TABLE VII

Failure to control the primary lesion	2
Primary lesion healed, secondary uncontrolled	10
Both primary and secondary uncontrolled	7
Remote metastasis	2
Operative mortality	4
	25

4. Base: 26 cases; 2 females, 24 males. Stage A, 3; Stage B, 8; Stage C, 11; Stage D, 4. Healing of the primary lesion was obtained in 30.7 per cent. Six patients, 23 per cent, are alive and symptom-free; 2 have died of extraneous disease, 1 after 9 months and 1 after 6 years without recurrence; sixteen, or 61.5 per cent, have died of the disease; 1 is untraced; and 1 is alive with recurrence.

TABLE VIII

There were 16 failures as follows:

Failure to control the primary lesion	3
Both primary and secondary uncontrolled	6
Remote metastasis	3
Operative mortality	3
Radium mortality	1
	16

COMPLICATIONS

In 53 of the cases no glands were present on admission. Seventeen of these later developed glands.

The complications encountered included involvement of the glands in 46 cases, involvement of the mandible in 2, remote metastasis in 8 (lung 4, kidney 1, sternum 1, ribs 1, rectum 1—probably separate lesion). Thirty-nine neck dissections were performed, with 38 positive pathological reports and one negative. In three bilateral neck dissections the pathological reports were positive on one side and negative on the other in all three. Five of the patients operated upon are alive and symptom-free; 30 have died of the disease, and 4 have died of extraneous disease. Further details regarding this aspect of the subject will be reserved for a later publication.

CONCLUSION

The strongest impression produced on one's mind as this work has been analyzed is the

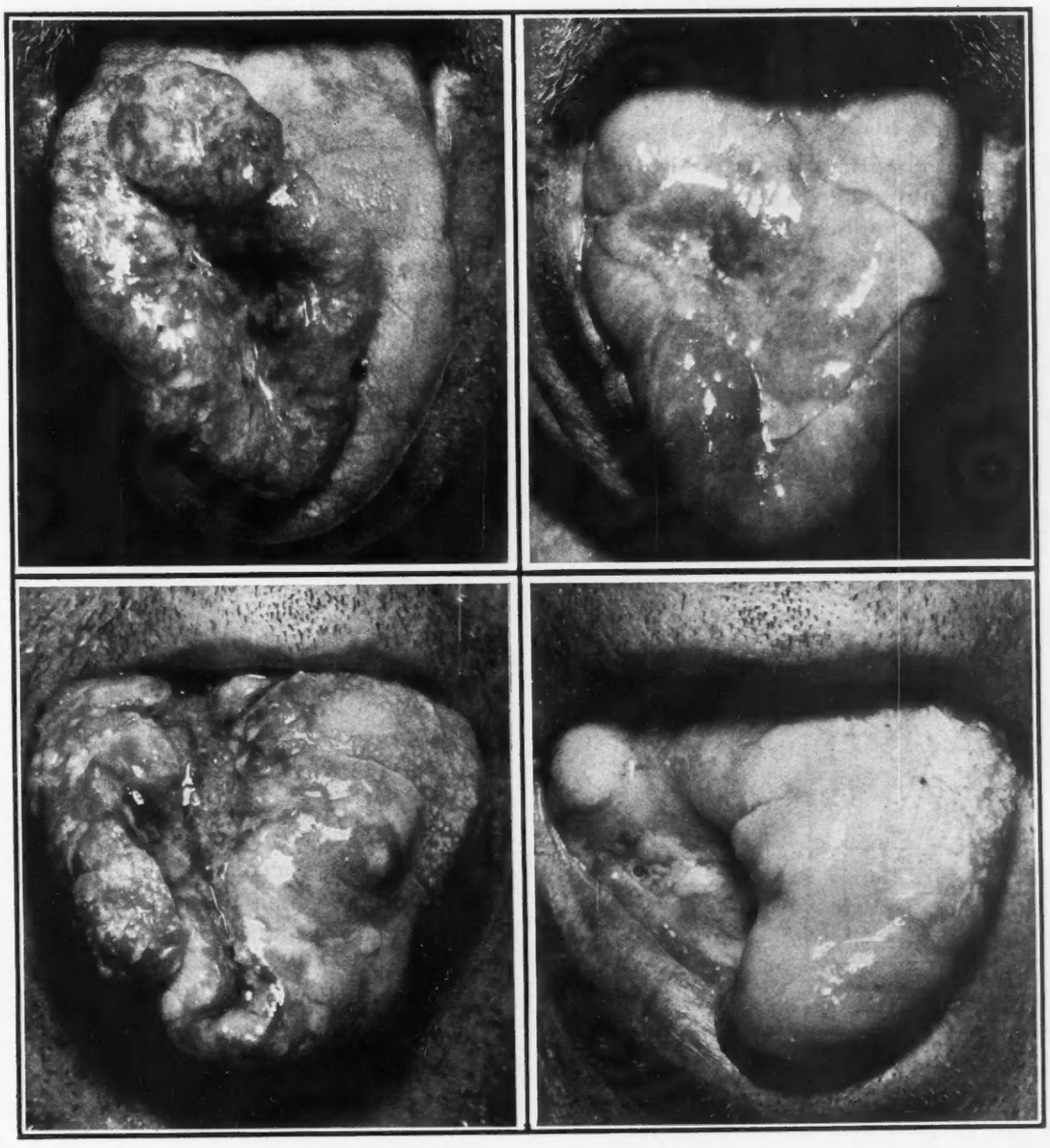

Fig. 3.—Stage III. "C"—Far advanced. Gross ulceration; extensive infiltration. Glands usually present, 10 per cent of such lesions were controlled.

Fig. 4.—Stage IV. "D"—Very far advanced. No cases in this stage were completely controlled by treatment.

urgent need for earlier diagnosis and treatment. In the present series 73 per cent were lesions which could only be described as quite advanced, though an attempt has been made to further subdivide them. In the early stage the percentage controlled by treatment is close to 60 per cent, and it is very obvious from the tables that the patient's chance of cure is rapidly diminished by every delay which is permitted.

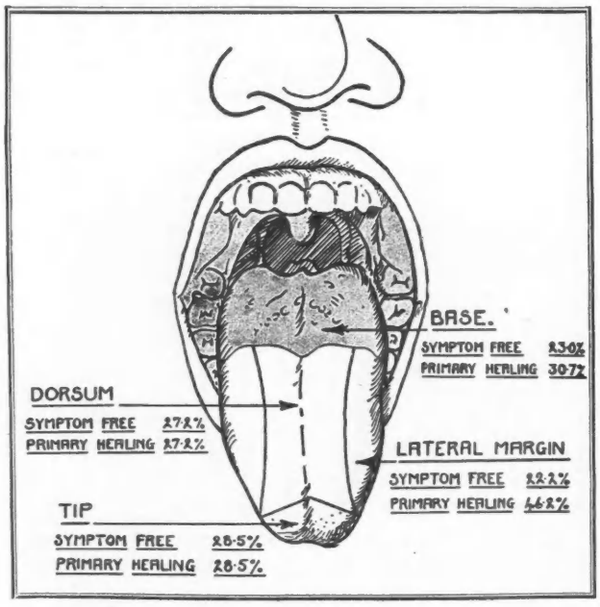

Fig. 5

In a person in middle life any lesion in any part of the oral cavity which fails to yield to ordinary methods of treatment within a reasonable time should be considered as being probably malignant, and its true character verified at the earliest possible moment. To keep any lesion on the tongue under observation until it has reached the stage shown in Fig. 4 cannot be defended on any grounds whatever. The presence of a positive Wassermann test should not be considered sufficient grounds for postponing accurate diagnosis and early treatment, owing to the frequent association of a positive Wassermann test and cancer of the tongue.

SUMMARY

1. The results of the treatment of 101 cases of cancer of the tongue are analyzed.

2. Twenty-five patients are alive and symptom-free (25 per cent).

3. Including those who died of extraneous disease without recurrence, the number in whom the disease was controlled is 34 (34 per cent).

4. Healing of the primary lesion by radiological treatment was obtained in 54 per cent of the whole group.

5. A discussion of the problem of glandular and other complications is reserved for future consideration.

THE RADIOLOGICAL TREATMENT OF CANCER

1929 – 1935

VI. INTRA-ORAL LESIONS (EXCEPT THE TONGUE)

BY G. E. RICHARDS, M.D., F.R.C.P.(C.)

Toronto

IN this group have been included lesions arising from the floor of the mouth, the lower alveolar ridge, the buccal mucosa, the superior alveolar ridge and the roof of the mouth, including both the hard and the soft palate. Lesions arising primarily in the tonsil or in the tonsillar pillars have been considered separately. Great difficulty is encountered in accurately determining the point of origin in many late cases and some earlier ones. Lesions arising, for example, in the floor of the mouth may involve the side of the tongue on the one side and the alveolus on the other; lesions arising close to the pillar of the tonsil may involve the buccal mucosa or the adjacent lateral margin of the tongue, or both. Hard and fast lines in classifying such lesions cannot be drawn, and a certain amount of overlapping is inevitable. Under such circumstances the lesions have been classified according to the maximum apparent involvement and the major problem presented in treatment.

Material.—The total number of cases treated during the period under review is 158, of which the point of origin has been: alveolus, 60 cases; floor of mouth, 30; buccal mucosa, 55; roof of mouth, 13.

From the standpoint of treatment the problem presented in each of these divisions is somewhat different, and there are technical objections to discussing them all in one category. The results will therefore be presented for the whole group, after which the details in each group will be reviewed briefly.

RESULTS FOR THE WHOLE GROUP

Of the total of 158 patients, 69, or 43 per cent, are alive and symptom-free; 5 are alive but not free of disease; 70, or 44.3 per cent, have died of the disease; 10 have died of extraneous disease, and 4 are untraced. The cases considered symptom-free are distributed in the four subdivisions as follows:

TABLE I

Region	*No. of cases*	*Symptom-free*	*Percentage*
Alveolus	60	21	35.0
Floor of mouth	30	15	50.0
Buccal mucosa	55	27	50.0
Roof of mouth	13	6	46.1

Influence of the stage of disease on results.—So much emphasis has been given the subject of early diagnosis in cancer of all forms that it becomes a matter of interest to enquire just how important it is to the patient whether treatment is undertaken at an early stage or how serious delay becomes.

In classifying our cases four stages have been recognized, and from a study of Table II, which follows, it appears that treatment during the early stage of the disease offers a prospect of a successful result in a comparatively high percentage of all cases, almost regardless of the point of origin. In the next two groups there does not appear to be so much difference in the results as might have been expected, although both have dropped to less than 50 per cent of the early group. Those classified as hopeless have proved to justify that description in every instance. It is difficult to see how the importance of early diagnosis and of early and proper treatment could be more effectively emphasized than by a careful study of this table.

One has been impressed also in this series by the observation that very few fatal recurrences have occurred after the second year. Within that period most of the complications and recurrences which have been encountered have occurred, and have either been successfully controlled or have been so serious as to prove fatal to the patient. Whether this is mere coincidence or due to the small total number of cases available for study is not apparent, but the observation has seemed to us of interest and of some value in prognosis.

TABLE II

RESULTS IN THE WHOLE GROUP ACCORDING TO STAGE OF THE DISEASE

Stage of disease	*No. of cases*	*Alive and well, symptom-free*	*Per-centage of total*
A.—Early	29	27*	93.1
B.—Moderately advanced .	65	27	41.5
C.—Far advanced	49	15	28.5
D.—Hopeless	15	–	–
	158	69	43.5

* 1 patient died of disease; 1, untraced.

I. LESIONS INVOLVING THE ALVEOLUS.—

Sixty of the cases were classified in this group and include those which either originated in the tissues covering the alveolus or later involved these tissues to such an extent as to constitute the major problem in treatment. Eight of the cases were "early"; 22 "moderately advanced"; 24 "far advanced"; and 6 "hopeless".

In this location the complication to be feared is not involvement of regional glands, as in other forms of oral cancer, but involvement of neighbouring bony structures by direct extension. Considering the intimacy of the anatomical relationship it is a matter for surprise that such direct extension is not more common than is actually the case. The complication, however, assumes added importance when it is known that malignant processes involving bone do not respond well to radium therapy, and that bone and the soft tissues close to bone are very easily damaged by radium, resulting in necrosis, sequestrum formation, and osteomyelitis, thus rendering applications of radium in the proximity of any bony structure one of considerable difficulty. Improvements in technique have lessened the risk from this source, but it still remains to a degree.

Results for the group.—Total number of patients, 60; 21, or 35 per cent, are alive and symptom-free; 32, or 53.3 per cent, have died of the disease; 3 have died of extraneous disease; 4 are untraced.

In those who died of extraneous disease the primary lesion was healed at the time of death, six months, eight months, and two years following treatment.

Table IV brings out the fact referred to previously, namely, that the disease is usually either brought under control fairly promptly or proves rapidly fatal, the majority of the deaths having occurred within the first two-year period.

TABLE III

RESULTS ACCORDING TO STAGE OF DISEASE

Stage	*No. of cases*	*Alive and well*	*Per-centage*	*Died of disease*	*Died of extraneous disease*	*Un-traced*
A.	8	7	87.5	–	–	1
B.	22	7	31.7	13	1	1
C.	24	7	29.1	13	2	2
D.	6	–	–	6	–	–
	60	21	35.0	32	3	4*

* None of these patients reported back as instructed, and we have been unable to obtain accurate information regarding them.

TABLE IV

FOLLOW-UP ACCORDING TO THE TIME ELAPSED SINCE TREATMENT

Time	*Alive and well*	*Died of disease*	*Died of extraneous disease*	*Untraced*
Under 1 year	–	16	2	4
1 to 2 years	3	14	–	–
2 to 3 years	10	2	1	–
3 to 4 years	–	–	–	–
4 to 5 years	3	–	–	–
5 to 6 years	3	–	–	–
6 to 7 years	2	–	–	–
	21	32	3	4

While it may not always remain true, it is probably a fairly safe working assumption. (See also Table VII.)

Complications.—(1) INVOLVEMENT OF GLANDS.—Having regard to the fact that 46 of the total of 60 cases were classified as being moderately or far advanced, it is interesting to find that in 35 cases no glandular involvement was present on admission, and in only two of these cases did glandular involvement later develop. Palpably enlarged glands were present in 24 cases on admission. The fact is also brought out, as shown in Table V, that in this type of lesion a very advanced primary may be present without a corresponding or indeed any involvement of regional lymphatics. Two of the hopeless cases had no glands present.

(2) INVOLVEMENT OF BONE.—As has previously been pointed out the close proximity of bony

TABLE V

Stage	*No. of cases*	*No glands on admission*	*Glands palpable on admission*	*Glands doubtfully present on admission*
A.	8	8	–	–
B.	22	12	9	1
C.	24	13	11	–
D.	6	2	4	–
	60	35 (58.3%)	24 (40%)	1

structures in both upper and lower alveoli introduces a new complication in the form either of direct invasion of the adjacent bone by the malignant process or necrosis of bone as a possible sequel to the radiological procedures undertaken for the cure of the disease. This is a field in which the closest cooperation between surgeon, radiologist, and dentist is essential. Malignant involvement of bone is one of the lesions highly resistant to radiological methods, and when it occurs treatment must almost always be a combination of radiotherapy and some surgical procedure. Radiotherapy may usually be counted upon to control the soft tissue involvement, but unless the patient is willing to submit to a subsequent and frequently quite radical surgical removal of the involved bone a final cure of the disease is impossible.

In the present series involvement of bone occurred in 20 cases, 4 of which were sequelæ to treatment, the remainder being active malignant invasion of bone. In the second group of cases the surgical procedures undertaken were an essential part of the direct attack upon the malignant disease, while in the former, though no less essential, they were plastic or reparative in nature, undertaken in cases in which the malignant disease had been controlled by radiotherapy.

Summary re causes of failure.—A study of the group for the purpose of discovering the causes of failure reveals that failures were as follows:

TABLE VI

	Cases
1. Involvement of bone	10
2. Uncontrolled primary alone	7
3. Uncontrolled glands alone	3
4. Both primary and secondary, uncontrolled	8
5. Remote metastasis	2
6. Treatment palliative in hopeless cases, or not completed	1
Total	31

While remote metastasis constituted the major factor and the direct cause of death in two cases, as shown in the table, this complication was also present and a contributory cause of death in 2 others, making a total of 4 cases out of 58 in this series in which remote metastasis occurred. The sites were: hip, 1; intestinal tract, 1; spine and lung, 1; spine and tibia, 1.

II. LESIONS INVOLVING THE FLOOR OF THE MOUTH.—

Thirty cases presented lesions arising primarily in the floor of the mouth. Six were "early"; 15 "moderately advanced"; 6 "far advanced"; and 3 "hopeless".

Results for the group.—Fifteen, or 50 per cent, of the patients are alive and symptom-free; 1 is alive but not free of disease; 12, or 40.0 per cent, have died of the disease; 2 have died of extraneous disease. There are no untraced cases in this group.

TABLE VII

RESULTS ACCORDING TO STAGE OF DISEASE

Stage	*No. of cases*	*Alive and well*	*Percentage*	*Under treatment*	*Died of disease*	*Died of extraneous disease*
A.	6	6	100	–	–	–
B.	15	6	40	1	7	1*
C.	6	3	50	–	3	–
D.	3	–	–	–	3	–
	30	15		1	13	1

* Accidental death three years after treatment without recurrence.

N.B.—Note that there is not a great difference in the results of treatment in groups B and C, but a very striking difference between both of these and group A, on the one extreme, and D, on the other.

TABLE VIII

FOLLOW-UP ACCORDING TO TIME ELAPSED SINCE TREATMENT

Time	*Alive and well*	*Under treatment*	*Died of disease*	*Died of extraneous disease*
Under 1 year	–	1	6	–
1 to 2 years	3	–	6	1
2 to 3 years	3	–	1	–
3 to 4 years	2	–	–	–
4 to 5 years	4	–	–	–
5 to 6 years	3	–	–	–
	15	1	13	1

Complications.—(1) INVOLVEMENT OF BONE.—In 4 cases the disease involved the mandible by direct invasion, requiring surgical excision, and pathological reports were positive. In 3 others plastic operations were required for removal of sequestra or partial excisions; in one additional case of malignant invasion no operative procedure was possible. These represent types of cases in which successful surgical treatment is essential to a cure, malignant invasion of bone of this type being recognized as one of the limitations of radiotherapy. An occasional failure is due to refusal on the part of the pa-

tient to submit to the necessary surgical procedure at the appropriate time.

(2) GLANDULAR INVOLVEMENT.—In 19 of the 30 cases (63.3 per cent) no glands were present on admission. In 3 of these glands later developed. Palpably enlarged glands were present on admission in 11 cases, (36.6 per cent)—"A" 3 cases, "B" 4 cases, "C" 4 cases.

III. LESIONS INVOLVING THE BUCCAL MUCOSA.—

In 55 of the cases the primary involvement was in the mucous membrane of the cheek. Of these 10 were "early", 25 were "moderately advanced", 16 were "far advanced", and 4 were "hopeless".

Results for the group.—Twenty-eight, or 50 per cent, are alive and symptom-free; 1 is alive, but not free of disease; 22, or 40 per cent, have died of the disease; 4 have died of extraneous disease. No cases are untraced.

TABLE IX

RESULTS ACCORDING TO STAGE OF DISEASE

Stage	*No. of cases*	*Alive and well*	*Per-centage*	*Under treatment*	*Died of disease*	*Died of extraneous disease*
A.	10	9	90.0	–	1	–
B.	25	14	48.0	1	7	3
C.	16	5	31.2	–	10	1
D.	4	–	–	–	4	–
	55	28	49.0	1	22	4*

* One of these patients died two years following treatment without recurrence of the primary disease, one of pneumonia six months following treatment, one of intestinal obstruction and cardiac failure after three months, the primary being still uncontrolled. In the fourth case exact information is not available regarding the condition of the primary; death was due to cardiac failure.

TABLE X

FOLLOW-UP ACCORDING TO THE TIME SURVIVED SINCE TREATMENT

Time	*Alive and well*	*Died of disease*	*Died of extraneous disease*
Under 1 year	4	17	2
1 to 2 years	7	2	2
2 to 3 years	6	2	–
3 to 4 years	4	1	–
4 to 5 years	2	–	–
5 to 6 years	3	–	–
6 to 7 years	2	–	–
	28	22	4

Again one's attention is directed to the diminishing frequency of fatal recurrences as time passes. Seventeen of the total of 22 deaths occurred under one year of admission, and only one fatal recurrence occurred after three years had elapsed. One patient previously referred to is known to be alive with recurrence, and is under treatment.

Complications.—(1) PERFORATION AND ORAL FISTULA.—Three cases at the time of first admission had advanced to such a degree that perforation through the cheek had occurred. One of these healed following external radiation and has remained healed.

(2) GLANDULAR INVOLVEMENT.—In 33 of the 55 cases (60 per cent) no glands were present on admission. In 2 of these glands developed later. In 2 cases glands were questionably present. Palpably enlarged glands were present in 20 cases (36.3 per cent)—"A" 9 cases, "B" 9 cases, "C" 2 cases.

IV. ROOF OF THE MOUTH.—

In 14 of the cases the primary involvement was in the roof of the mouth, 13 being carcinomata and 1 very extensive melanotic sarcoma. This patient died of pneumonia a short time following the completion of treatment by teleradium, the disease being uncontrolled.

Results for the group.—Thirteen of the patients had carcinomata, and 6 of them, or 46.1 per cent, are alive and symptom-free; 2 are alive but not free of disease; 5 have died of the disease.

TABLE XI

RESULTS ACCORDING TO STAGE OF DISEASE

Stage	*No. of cases*	*Alive and well*	*Per-centage*	*Under treatment*	*Died of disease*
A.	5	5	100.0	–	–
B.	3	1	33.3	1	1
C.	3	–	–	1	2
D.	2	–	–	–	2
	13	6		2	5

All of the deaths have been due to the disease (including one post-operative death), and have occurred within the first year. In one case a recurrence or re-activity of a lesion has developed after four years, but has again responded to treatment.

Complications.—In 9 cases no glands were present on admission. Of these one later developed glands. Two cases presented palpably enlarged glands on admission, one being moderately advanced—"B"—and one far advanced —"C".

The involvement of glands constituted the only complication encountered in this group of cases, the number of which is too small to have much significance. One of the patients refused any treatment and died of the disease in four months. The second was treated radiologically owing to the fact that his primary lesion was considered incurable and radical surgery therefore contra-indicated. This patient survived 9 months. The third was treated by neck dissection following control of the primary lesion, and was an operative mortality.

SUMMARY

1. The results of treatment of 158 cases of intra-oral cancer are analyzed.

2. In the treatment of the primary lesions, radiological methods were the principal methods employed; the treatment of glandular secondaries and bony involvement was primarily surgical, radiological procedures being used as adjuncts to surgery in dealing with these complications.

3. The most important consideration affecting the final result of treatment appears to be the stage of disease at which treatment is undertaken. Of 29 patients who were treated during the "early" stage of the disease, 27 are free of disease, 93.1 per cent. Of 15 cases on the other extreme, in which the disease was very advanced, all were failures.

4. Seventy-two per cent of the patients treated were in an advanced stage of the disease when first seen, which seems far too high considering our present knowledge of cancer and the facilities available for accurate diagnosis.

5. The complications encountered were glandular secondaries, involvement of bone, and remote metastasis. The detailed discussion of this aspect of the problem is reserved for special consideration later.

ENDOMETRIAL HYPERPLASIA—A CLINICAL ENTITY*

BY E. MURRAY BLAIR, M.D., C.M.

Vancouver

DURING the past few years a new diagnosis has appeared in the gynæcological firmament. I believe it is fair to say that 6 years ago the entity "endometrial hyperplasia" was little known to the majority of my hearers. Yet in 1934 in the Vancouver General Hospital alone this finding was reported from the pathological department some 200 times. The subject has surely dominated the field of gynæcology in literature in recent years. So spectacular has been the appearance of this now common entity that I think some discussion of the matter may prove of value.

In 1900 Thomas Cullen, in a treatise on cancer of the uterus, described a benign hyperplastic process of the endometrium, non-inflammatory in origin, and gave it the name "hyperplasia of the endometrium". The true meaning of the finding took nearly thirty years to unfold. In 1908 the histology of normal menstruation was put on a sound basis by Hitschman and Adler. In 1923 the story of the sex hormones began to be elaborated, and the application of these to the changing uterine mucosa was gradually established by Schroeder, Myer, Zondek, Frank, Novak and many others. Such was the avenue of approach through which endometrial hyperplasia came down to us as a clinical entity.

In order to grasp the significance of this condition three things seem to me essential: (1) a picture of the physiology of normal menstruation; (2) a picture of the physiology of ovarian hormone production; (3) a picture of the pathological (anovulatory) cycle which is productive of endometrial hyperplasia.

PHYSIOLOGICAL HORMONE PRODUCTION IN THE OVARY

Fig. 1 represents an average 28 day menstrual cycle. It is divided into quarters of seven days each. The cycle here begins at 6 o'clock and moves clockwise. The first period is that of menstruation, 5 days. Following that is a period of follicular ripening, 9 days. In this period a follicle proliferates, approaches

* Presented before the Section of Obstetrics and Gynæcology, Annual Meeting, Canadian Medical Association, June 25, 1936, at Victoria, B.C.

the periphery of the ovary, protrudes beyond the periphery, and finally bursts, extruding its egg in the phenomenon of ovulation. Ovulation then usually takes place some 12 to 16 days after the beginning of menstruation. Following ovulation is the formation of the corpus luteum. This body remains at the seat of ovulation some 10 to 12 days, then degenerates and disappears, whereupon menstruation occurs.

Fig. 2 represents the ovarian hormone production during such a cycle. During the follicular ripening period the follicular or œstrogenic hormone is formed in the follicle. Following ovulation the hormone progestin is formed in the corpus luteum. The corpus luteum with its hormone persists for some 10 to 12 days, then degenerates. Menstruation follows. There are only two ovarian hormones, œstrin formed before ovulation, and progestin, after ovulation. It must be remembered that some œstrogenic hormone is found in the corpus luteum together with progestin.

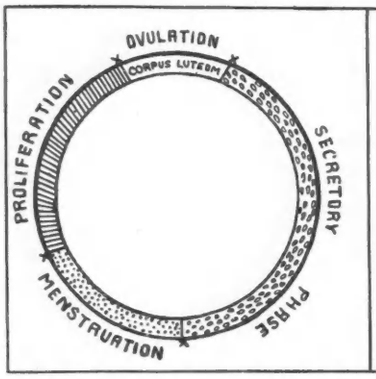

Fig. 1.—Physiology of normal menstruation.

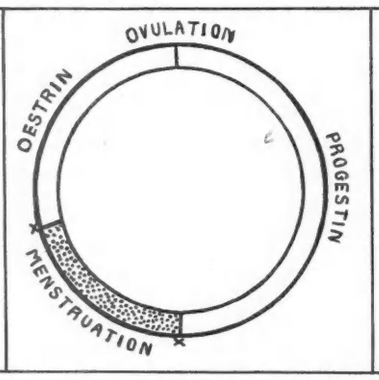

Fig. 2.—Physiology of ovarian hormone production.

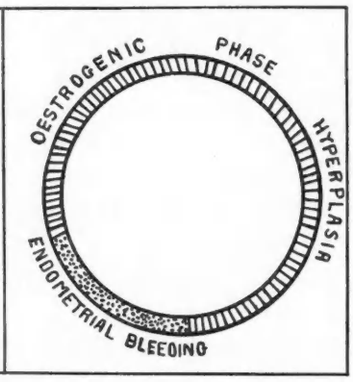

Fig. 3.—Pathological (anovulatory) cycle which is productive of endometrial hyperplasia.

WHAT IS THE APPARENT CAUSE OF THE ENTITY "HYPERPLASIA"?

Fig. 3. In hyperplasia of the endometrium there is found one significant and practically constant factor, *i.e.*, the absence of corpus luteum, hence no progestin and no secretory stage. There is however a hyperplasia or overgrowth of the endometrium caused by an apparent over-production of the follicular œstrogenic hormone. It would then be reasonable to deduce that ovulation has not taken place in these cases, but that instead the follicle is formed and continues to produce its hormone without subsequent follicle rupture, hence without subsequent corpus luteum and progestin formation.

The chief ovarian change is the absence of corpus luteum, but another extremely common if not invariable accompaniment is the presence of one or more large follicular cysts (Fig. 4). It is the content of these cysts, carrying as they do quantities of the œstrogenic hormone, which stimulates the normal endometrium beyond its normal interval stage to the hyperplastic stage. Endometrial hyperplasia is then an overgrowth of the normal endometrium because of an overabundance of œstrin.

A hyperplastic endometrium is a bleeding endometrium, as a general rule. It is true that all hyperplastic endometria do not bleed, but I believe that they are the exceptions to the rule.

Fig. 4.—Follicular ovarian cysts.

It is because of the bleeding that this entity interests us as clinicians.

It is probable that the reason ovulation did not take place was because the follicle was unable to rupture the surface of the ovary and so extrude the ovum. Later, follicles formed in subsequent months may meet the same fate, and so multiple follicular cysts may arise, each continuing to discharge its follicular or œstrogenic hormone into the circulation and causing an overgrowth of its follicular phase. Such a condition of the endometrium is known as endometrial hyperplasia.

Just what causes such an endometrium to bleed is not known. Novak speaks of an unknown bleeding factor. Many point to multiple minute areas of necrosis in the hyperplastic endometrium. Late studies seem to point to anterior pituitary control. The fact remains that from a clinical standpoint it does bleed,—at times very seriously. Such uterine bleeding in pelves that present no gross or demonstrable lesions has always been with us. We have referred to this as essential uterine hæmorrhage, fibrosis uteri, or menorrhagia of unknown origin. As it very often appears at or near the menopause, such bleeding has always brought sharply to our minds the possibility of cancer of the corpus. With this thought uppermost in our minds it is I think but natural that the general consensus seems to be that the bleeding uterus must be removed forthwith. And this belief is generally harboured despite the fact that endometrial hyperplasia is the result of an ovarian hormone imbalance.

I base this belief on a study of the hysterectomy statistics at the Vancouver General Hospital for the year 1934. In all 161 hysterectomies were performed. The various pathological reasons are shown in Table I. I find that the figures presented coincide fairly well with inquiries I have made in teaching hospitals in the east and south. It is apparent from the records that 31 uteri, or about 20 per cent, were removed because of endometrial hyperplasia only. This statement can be made because every uterus removed must be and is subjected to the microscopic eye of the pathological department, and our figures are based on pathological findings, not clinical. Every uterus in this group was a normal uterus with a hyperplastic endometrium. Each case was, I think, simply the result of continued activity of the follicular or œstrogenic hormone with no resulting progestin. Is it not fair to say that each uterus was removed because of hormone imbalance? Each of these 31 uteri was removed because of uterine bleeding, the majority at or near the menopause. From a clinical standpoint the pathological department found a normal uterus with a hyperplastic endometrium.

TABLE I

HYSTERECTOMIES, VANCOUVER GENERAL HOSPITAL, 1934

For:	
Endometrial hyperplasia only	31
Fibromyomata	83
Cancer corpus	6
Cancer cervix or ovaries	6
Other causes	35
	161

Some consideration of these 31 hysterectomies for endometrial hyperplasia only may prove of interest. In the first place they constitute about 20 per cent of all the hysterectomies performed for any reason in 1934. The patients in question spent a total of 600 days in the hospital. There were some complications, some morbidities, but no mortalities. The average age was 39 years; 28 patients were over 35 years. Each uterus in this study was removed because of the pathological entity, hyperplasia of the endometrium, and each case had as its primary symptom, vaginal bleeding. Besides the 31 cases cited above there were 3 more in which the sole pathological entity was endometrial hyperplasia, but the uteri were not removed because of the bleeding. Two were removed because of prolapse, one because of a former operation with resultant adhesions and pain. These uteri then were not removed because of bleeding, though hyperplasia was found. This seems to substantiate the belief among some authors that all hyperplasias do not bleed. The following interesting facts are gleaned from the records. (1) In no case was a diagnosis of endometrial hyperplasia made before the operation. (2) A mistaken preoperative diagnosis of fibromyomata was made in more than 50 per cent of the cases. (3) In 12 cases the ovaries were either attached to the specimen or their condition reported by the surgeon. In 11 there were single or multiple cysts; in one the ovaries were reported as

normal. In 19 the condition of the ovaries was not reported. (4) In none of the cases were we able to find evidence of any preliminary microscopic study of the endometrium.

It will seem unfortunate to many of us that these women had to be subjected to a major operative procedure with all its discomfort, all its risk, all its expense, with such an etiology. Let us reserve any discussion of the matter until all the evidence we have regarding endometrial hyperplasia is considered. As hyperplasia of the endometrium is so very common in fibromyomata cases, we have studied the 83 hysterectomies for fibromyomata during the same year in this hospital. There is I think a good deal of additional information to be obtained from such a study.

FIBROMYOMATA

The subject of endometrial hyperplasia is so markedly interlocked with that of fibromyomata that any discussion of the former from a clinical standpoint without including the latter must be incomplete.

There were 83 hysterectomies for fibromyomata in the Vancouver General Hospital in 1934. Of these, 67 showed definite hyperplasia of the endometrium, or 81 per cent. It should be pointed out that 10 of the 16 uteri which did not show hyperplasia were in women between the ages of 47 and 79 years, and mostly beyond the years of ovarian activity. It is not surprising then that their endometria are reported as "chronic endometritis" and "atrophic", not hyperplastic. There were however a few endometria in women beyond the menopause which were distinctly hyperplastic. The chief complaint which led to examination and subsequent operation was vaginal bleeding in 59 of the 83 cases, or 71 per cent. It is quite possible in some of these older age bleeding cases that a small granulosal cell tumour of the ovary has been overlooked.

Such a uniform finding of hyperplasia among fibroid uteri is surely no coincidence. Indeed, there seems to be a close relationship between these two groups of cases. Each is a group of bleeding uteri in nearly every case; each has the same sort of bleeding surface in the majority of cases—a hyperplastic endometrium; each appears at about the same time in life; and each is treated in the same radical way. All things considered, it may be reasonable to ask, "does the same etiological factor which causes endometrial hyperplasia cause fibromyomata also?" In other words, are fibromyomata of the uterus as well as endometrial hyperplasia caused by hyperœstrinism?

The theory was first brought forward, I think by Witherspoon, a few years ago and is to me, most interesting. When an over-production of œstrin is sufficient to produce a pathological stimulus, why should this stimulus be limited in its action to a single layer of the uterus? Under the stimulation of growth and reproduction the uterus as a whole is involved, not just the endometrium. Also be it remembered that œstrin is known to be a very distinct factor in uterine growth as well as activity. Is it not reasonable to believe, then, that this hyperœstrin-production causes myometrial as well as endometrial reactions? It is at least possible that hyperplasia is the early response to œstrin stimulation and fibromyomata a more latent response.

There are doubtless many causes for failure of the follicle to rupture. As the woman becomes older the cortex of the ovary becomes firmer and of a denser consistency, and of equal importance is the reaction of the ovary to infection from any cause, with its resultant increased cortical density, exudate, adhesions, etc. It has been recognized for many years that one cannot speak of salpingitis as an isolated entity, that almost invariably the ovary also is involved in the process. Infection, then, as first pointed out by Frankel, may well play an important part in the formation of hyperœstrinism, with resultant hyperplasia and perhaps fibromyomata.

In support of this theory we should consider the negro race on this continent because of the fact that they are so extraordinarily prone to uterine fibromyomata. In the Charity Hospital, New Orleans, it was recently reported that though the admissions to the gynæcological service are about evenly divided between the coloured and white races 90 per cent of the fibromyomata were found in negroes. Miller believes that nearly 50 per cent of all negro women over 50 years have fibromyomata.

There is also a great prevalence of pelvic infection among these negro women. Seventy per cent of all pelvic infections at Charity

Hospital were in negroes. It is usual in the East to warn students about performing interposition operations or vaginal hysterectomies upon negroes because of the prevalence of chronic adnexal disease. In Bellevue Hospital in New York we believed, fifteen years ago, that fibroids and pus tubes were almost concomitant in the negro.

The common explanation of fibroid growths in the negroes is that they are a racial inheritance. Keloid growths in the skin are also extraordinarily prevalent in the black. It is perhaps natural that these two entities have been listed together as racial inheritances. In the first place there is no evidence in medical literature that keloids and fibroids are related. Again, keloids have been used by the natives of Africa for cosmetic adornment for centuries, but the early writings of medical missionaries in Africa stress the rarity of neoplasms in the black. Others speak of the rarity, even the absence, of malignancy in the aboriginal black. Surmont and Suva (medical missionaries), after a lifetime among the blacks of Africa, report 5 cases of fibroids of the uterus, 3 at autopsy, and each with accompanying cystic ovaries. This report was in 1927. It is perhaps then fair to say that fibroid is not, like keloid, a racial characteristic, as the forbears of the American negro did not in their primitive state exhibit fibroid tumours of the uterus.

It has been said that fibroids of the uterus were rare among the Polynesians until the advent of the white traders. Fibroids then seem to appear with the tide of civilization, and with them march hand in hand the spread of pelvic infection. When the surface of the ovary becomes so affected that the follicle cannot rupture, then is there a gradual increase in œstrin in the circulation with no progestin to act as a buffer. Then appears the primary over-stimulation of the endometrium, endometrial hyperplasia, and the ultimate overstimulation of the myometrium, with gradual fibroid formation. It is of some significance that fibromyomata are seen only in our own species, never in the lower animals. Even the higher apes are said to be relatively immune. We should be reminded again that a number of the organisms which attack mucous membranes, particularly the gonococcus, are active only in our own species.

As has been said already, it is not suggested that infection is the only cause of endometrial hyperplasia or fibromyomata. We have but to refer to the cases with no suggestion of pelvic infection, perhaps in young virgins, and the members of religious sisterhoods who may occasionally exhibit fibroid tumours of the uterus. Any entity that inhibits ovulation may cause it, and pelvic infection is but one of them, and I think a common one.

The rapid growth of fibromyomata during the later months of pregnancy is often observed. It is probably the reaction to stimulation caused by the physiological hyperœstrinism at that time.

Finally we should be reminded that if the fibroid uterus can be carried to the menopause the bleeding stops, and gradually the tumours tend to regress and even disappear. What has happened? The ovary has ceased to function. The follicle is no longer formed each month, œstrin is no longer produced, and so the stimulation to endometrium and myometrium is removed. The resulting hyperplasia and fibromyomata tend to disappear. Should the menopause be brought about artificially by radiation exactly the same phenomenon obtains.

The age-old query as to what makes a fibroid bleed might well be changed to "does a fibroid bleed?" The patient presents herself because of vaginal bleeding. On examination an enlarged uterus with irregular outline is correctly diagnosed as multiple fibroids, and as the fibroid uterus is bleeding a hysterectomy is advised. More than that, there are men here who can state with some assurance that they have seen a fibroid bleed. The patient with a history of prolonged menses, inter-menstrual bleeding, bleeding after coitus, is found to have a tumour presenting in the cervix and protruding into the vagina. On touching the tumour it is seen to bleed readily. A number of factors must be considered. The bleeding may be caused by a hyperplastic endometrium covering the polyp; the bleeding may be from within the uterus; and lastly a polyp, be it fibroid or otherwise, in direct contact with the vaginal wall or its secretions, may readily become eroded. Any raw surface may bleed. It is my contention in support of this theory that a fibroid of the uterus *per se* may very possibly neither bleed nor cause bleeding.

It seems reasonable to contend that in this "fibroid" group, as in the "hyperplasia only" group, the bleeding surface is the endometrium only, and that the fibroids *per se* have in the great majority of cases little if anything to do with bleeding. Indeed if the theory carry some modicum of fact the "fibroid" group are simply the "hyperplasia only" group, but of longer standing. The hyperœstrinism has now affected the myometrium as well as the endometrium.

With the idea of either supporting or refuting this etiological theory a rather careful review of the fibroid uteri removed at the Vancouver General Hospital during 1934 was undertaken. The average age in this group was 45, as compared to 39 in the "hyperplasia only" group. The following factors were studied: (1) the type of endometrium in the uteri removed; (2) the relation of the fibroid or fibroids *per se* to the endometrium from the standpoint of bleeding; (3) the histories from the standpoint of early pelvic infection; (4) the reports on the condition of the ovaries either by the surgeon or the pathologist, or by both.

The endometrium.—As has already been said 67 of the 83 uteri showed hyperplasia, or 81 per cent. In 16 the endometrium was diagnosed as exhibiting chronic endometritis. It is interesting to note that only 4 of the 16 chronic endometria were in patients complaining of vaginal bleeding. In the other 12 there was no bleeding. Ten of these 12 were beyond the menopause. There were however 4 uteri removed because of vaginal bleeding which did not exhibit endometrial hyperplasia.

The relation of fibroids to the endometrium.—It was interesting to note that in only 30 of the 83, or 36 per cent, of the uteri removed did fibroid tumours in any way impinge on the endometrium. Therefore, in 53, or 64 per cent, of the uteri the tumours had no apparent relation whatsoever to the endometrium. It would seem to strengthen the argument that fibromyomata of the uterus *per se* do not cause uterine bleeding. Whether a submucous fibroid may or may not bleed as the result of various extrinsic factors is another matter.

The histories from the standpoint of early pelvic infections.—It was interesting to note that 30, or 36 per cent, of the 83 fibromyomata uteri had undergone some former operation, and that curettage was by far the commonest procedure. The histories gave nothing as regards early pelvic infection. They were not taken with this idea in mind, and so it was natural that only by chance and but rarely was any note made of previous pelvic inflammation. But the number of times that ovaries were reported as "embedded in a mass of adhesions" or "firmly adherent to the posterior surface of the broad ligament" was evidence that pelvic infection had passed that way in a goodly number of cases. I believe that if we took our histories of fibromyomata cases with previous pelvic infection in mind we would be surprised how often infection would appear as an apparent forerunner of the tumours.

Reports on the condition of ovaries by surgeon or pathologist or both.—It is pretty certain that every surgeon examines the ovaries before performing hysterectomy. (All the hysterectomies performed in the Vancouver General Hospital in 1934 were abdominal). It is unfortunate that in 33 of the 83 cases there was no report on the condition of the ovaries, either by the surgeon or pathologist. Of the 50 cases reported, in 14 the ovaries are reported as normal, and in 36 as exhibiting single or multiple cysts. At first sight this is a very small percentage and in no way supportive of the theory that follicular ovarian cysts cause endometrial hyperplasia and fibromyomata in the uterus. The real facts are, however, I think, that our surgeons' reports on the state of the ovaries found at operation are so incomplete and sketchy as to be valueless. Those reports which we have from the pathologist are too few to carry much weight, but they all showed multiple follicular cysts.

We have to report one very interesting finding by the pathologist in the routine examination of those ovaries which were presented with the uterus. No less than 10 luteal cysts were reported. Such a finding is not compatible with the accepted theory of hyperplasia. However they were always found in conjunction with multiple follicular cysts. It may be that there is so great a preponderance of œstrin in the system by virtue of prolonged retention cysts in the ovaries that the occasional ovulation and resulting luteal body and progestin formation had little or no effect on the endo-

metrium. In view of this theory it is readily understood why the "fibroid" uterus is a sterile uterus. The fundamental principle in the entire sequence of events is failure of ovulation. On the other hand fibroid uteri occasionally do become pregnant. Their ovaries then must ovulate on occasion—hence the unusual picture of a corpus luteum in the presence of hyperplasia and fibromyomata.

SUMMARY

An endeavour has been made to present to you a general survey of the hysterectomies performed in our hospital during the year 1934 for endometrial hyperplasia only, and for fibromyomata uteri. We have paid particular attention to the pathological entity "endometrial hyperplasia". We have presented two groups of cases wherein this entity has played an important part: (1) 31 hysterectomies in which endometrial hyperplasia was the sole pathological entity; (2) 83 hysterectomies for fibromyomata uteri in which endometrial hyperplasia was found in 81 per cent of the cases.

We have endeavoured to define and explain endometrial hyperplasia. A theory has been offered which suggests that the hyperplasia of the endometrium and the more latent fibromyomata of the myometrium are caused by the same etiological factor—hyperœstrinism. The question of chronic pelvic inflammation as a factor in failure of the ovary to ovulate with subsequent overproduction of œstrin is brought forward. The findings in this series strongly suggest that the fibroid *per se* may well have little or nothing to do with the bleeding. That the bleeding surface in both groups is the endometrium, and that endometrium is hyperplastic in the great majority of cases.

The relation of the ovaries to the endometrium cannot be determined satisfactorily in this study for the very good reason that in about 50 per cent of the cases, considering both groups, there is no report.

CONCLUSION

1. With advancing knowledge as to a very common cause of bleeding in the uterus of the patient at or near the menopause it is suggested that our attitude toward the treatment of these people must undergo some change.

2. Our attention must be drawn more toward the ovary and less toward the uterus in a search for the cause of the trouble.

3. Preliminary biopsy of the endometrium should have a greater place in our preoperative calculations than of yore.

4. Thorough endometrial biopsy (curettage) plus artificial menopause should have a greater place in the treatment of selected cases than is generally practised.

5. Supplementary endocrine therapy should continue to attract the profession, in the hope that it may eventually prove more satisfactory than at present.

EUNARCON ANÆSTHESIA.—K. Mensing gives an account of his experiences with 100 cases of eunarcon anæsthesia since it was first introduced in his hospital at the beginning of 1935. Eunarcon is a 10 per cent solution of the water-soluble sodium salt of C-C-isopropyl-*B*-bromallyl-N-methylmalonylureids. The injections induced in almost every case a superficial respiration which not infrequently culminated in a complete cessation of respiration while the pulse remained good. To resort promptly to coramin and CO_2 on this indication is unjustly to give such treatment the credit for a return of the respiration, which will be spontaneous if nothing is done. Provided the pulse is good, the superficial character of the respiration may be safely ignored. The anæsthesia proved almost invariably satisfactory, but in one case vomiting followed the return of consciousness, and in another there was evidence of irritation of the kidneys possibly traceable to the anæsthetic. A third mishap was fatal. The patient was a woman, aged 76, suffering from asthma and requiring a general anæsthetic for the setting of a fracture of the neck of the femur. She had been given only 4½ c.cm. of eunarcon, when her pulse suddenly became thready. In spite of intravenous injections of coramin and artificial respiration, death ensued. In the absence of a post-mortem the cause of death could not be established beyond doubt, but the author suspects that the drug may have been given too rapidly, and he now injects it so slowly in patients over 45 that only 0.5 c.cm. or less is administered during the first minute. He also refuses to give eunarcon to patients suffering from peritonitis, severe diabetes, or disease of the parenchyma of the liver.—*Deut. med. Woch.*, 1936, p. 970. Abs. in *Brit. M. J.*

HÆMORRHAGIC ENCEPHALITIS FROM NEOARSPHENAMINE IN PREGNANCY*

(REPORT OF A CASE WITH UNUSUAL WIDESPREAD VASCULAR PARALYSIS)

BY FRANK E. CORMIA, M.D.

Montreal

A RECENT fatality from neoarsphenamine in a young, generally healthy, pregnant woman with clinically latent syphilis has raised the question of the influence of pregnancy on the development of so-called "hæmorrhagic encephalitis" following the use of the arsphenamines. A case with an obscure clinical course and with pathological findings of unusual interest will first be summarized, after which the available literature will be examined, with a view of clarifying the course and treatment of the syndrome and of determining whether or not common predisposing factors can be identified and eliminated.

CASE

J.S., aged 23 years, was first seen at the dermatological clinic in the fifth month of her second pregnancy. She had been previously examined in the Pre-natal Maternity Clinic, and was found to have a strongly positive blood Wassermann reaction.

The *personal history* was good. Marriage had taken place thirteen months previously. Five months later, after a mild fall, she had a miscarriage. The pregnancy was of four months' duration.

The *family history* revealed that the mother died of tuberculosis at the age of 27; the father had active tuberculosis.

The duration of the present trouble was unknown. There were no late manifestations. No specific treatment had been given. The spinal fluid had not been examined. There were no referable symptoms.

The *physical examination* was essentially negative. There was a slight prominence of the thyroid, but no symptoms suggesting hyperthyroidism were present. The lungs were clear. The liver and spleen were not palpable. The heart was not enlarged. The heart sounds were of good quality at the apex. The pulmonic second sound was ½ greater than the aortic second. There was a rough, but not loud, systolic murmur at the second left interspace. It was faintly heard in the corresponding right interspace. The examination of the nervous system was negative. The mentality was excellent.

The impression at this time was, that the patient had latent syphilis. Blood was drawn for another Wassermann test, and the patient instructed to return in two days. The Wassermann was again found to be strongly positive, and treatment was instituted with an oil suspension of metallic bismuth (bismuth) in a dosage of 0.5 c.c. (one-third of the adult dose). After a five day interval she was seen again, and bismuth, 1 c.c., and novarsenobenzol, 0.3 g., were given. One week later another injection of bismuth 1 c.c. and novarsenobenzol 0.45 g. was given. The preliminary treatment with bismuth was comparatively short, but it was felt that novarsenobenzol was essential for the life and health of the baby. The dosage of novarsenobenzol was raised to 0.45 g., as the patient was a larger than average woman. The overlapping of injections was to have been stopped the following week, with weekly continuation of the intravenous medication alone, until delivery.

Two days after the last injection she was said to have developed a fever of 101° F. There was a history of generalized body pains following the last injection. The following day she became slightly delirious. When seen by the visiting intern of the Maternity Section she seemed normal, but as he was leaving she suddenly became unconscious and cyanotic and was taken to the hospital. The urine analysis showed a faint trace of albumin and two granular casts.

Morphine sulphate, ¼ gr., was given, but she gradually became excited. Restraint of any kind made her worse. Soon she began to tear her clothes, was restless, and uncooperative. She apparently recognized her relatives, but answered questions only by "yes" or "no". She seemed disoriented. After a six-hour interval of comparative calm, she suddenly developed a convulsion. This first appeared on the right side, but rapidly became generalized. It soon subsided into a rigid spasm and deep coma. The blood pressure was 136/50. The leucocyte count was 21,000. The urine showed a heavy trace of albumin and numerous granular casts. She was restless. There were increased movements, scratching, and rolling of the eyes. Two hours later there was another convulsion. The blood pressure was 160/50. Three short convulsions followed at intervals of 45, 90 and 20 minutes. One-half hour after the last convulsion the pulse became very rapid, the temperature was 105° F., and the patient ceased breathing. Paraldehyde rectally, sodium luminal intravenously, and adrenalin subcutaneously were tried, but seemingly had no effect on the progress of the symptoms. A complete post-mortem examination was made eight hours after death.

SUMMARY OF THE PATHOLOGICAL FINDINGS

There was a limited syphilitic aortitis. The right sinus of Valsalva showed pearly grey scarring and puckering, which extended over the adjacent aorta for a distance of 1.5 cm. and involved the origin of the right and left aortic cusps. There was a septic splenitis.

The lungs were hyperæmic and there was a bilateral productive pleurisy.

The liver was moderately enlarged and showed parenchymatous degeneration and focal hyperæmia.

The cerebral convolutions of the brain were slightly flattened. The leptomeninges were dry. The vessels at the base were free and well preserved. The pons and the medulla were pale.

Sections cut transversely about 2 cm. above optic chiasm (see Fig. 1), showed marked softening and swelling of symmetrical parts of the cerebral convolutions. This involved the hippocampal gyri, which contained many punctate hæmorrhages. On the left the adjacent convolution of the frontal lobe showed a similar picture. The cerebral peduncles showed marked engorgement of the vessels and perivascular red discoloration. A few similar red punctate areas were scattered throughout the brain substance.

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Fig. 1.—Horizontal section of the brain about 2 cm. above the optic chiasm.

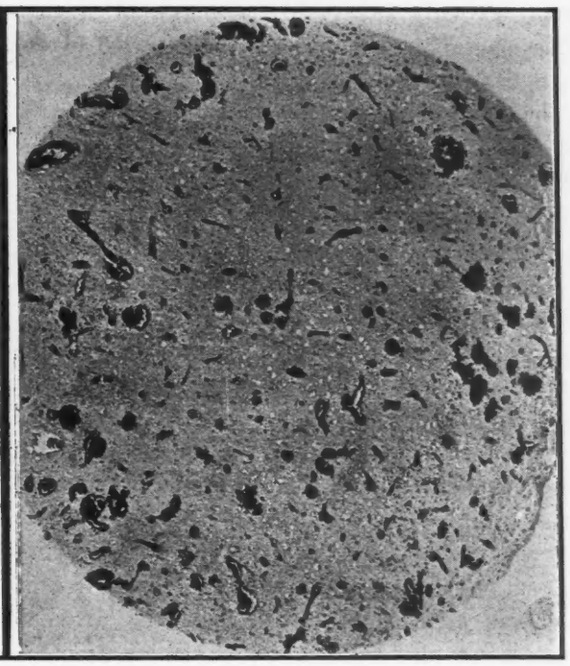

Fig. 2.—Section through the area of greatest damage in the temporal lobe.

All the intracranial arteries and large veins were engorged with *cruor clot*. No gross thrombi were seen. The left hippocampal convultion was slightly wider and softer than the right, its greatest transverse diameter being 2 cm., while the right was 1.6 cm.

Microscopical findings. — Temporal lobe, cerebral cortex; there were intense engorgement of the capillaries with red cells and leucocytes, and extensive focal perivascular extravasations with slight fusion in some areas. In places there was a narrow zone of necrosis surrounding the central thrombosed capillary. Most of these areas had a peripheral zone of red cells, (the so-called "ring hæmorrhage"). There were many thrombi in the terminal districts, consisting of serum, fibrin and leucocytes; and marked vacuolation, swelling and fragmentation of surrounding glial fibres were associated.

Frontal lobe, cerebral cortex: there were scattered thrombi in small vessels throughout the layers of the grey matter, with few perivascular red cells. The larger arteries and veins were dilated with red cells, and many were surrounded by clear vacuolated areas of brain tissue.

Optic thalamus: the section showed a similar picture of capillary thrombosis, with less numerous perivascular hæmorrhages.

Lenticular and caudate nuclei: the sections showed an intense engorgement of the larger arteries and veins. No definite perivascular hæmorrhages were seen in the sections examined, and the capillaries were almost free of blood.

Pons: both sides were involved. There was an intense engorgement of capillaries with red cells. In districts these extended into the surrounding tissue, to form partly fused foci. Many capillaries contained serum, leucocyte and fibrin thrombi. The larger arteries and veins were well preserved. There was slight vacuolation of pale staining glial cells and fibres surrounding these vascular lesions.

Medulla: there were numerous capillary thrombi, consisting mostly of serum and red cells. In some places red and white cells surrounded these capillaries. The endothelial cells were swollen, fused and poorly defined. The larger arteries and veins in the meninges were well preserved.

Liver: the liver cells were swollen, with a pale granular cytoplasm, and poorly defined borders. There were abundant pale serous material and hæmolyzed red cells between the liver cells. In some places only the nuclei remained. Scattered leucocytes surrounded the bile ducts.

Spleen: the pulp was filled with partly hæmolyzed red cells and many polymorphonuclear cells. The lymph follicles were compressed by this engorgement.

Adrenal glands: there were marked passive hyperæmia and an adenomatous arrangement of the cortical cells (as is commonly seen in pregnancy), which had an abundant vacuolated cytoplasm filled with fat.

Fetus: there were many petechial hæmorrhages, mostly in the serous cavities. The gross picture suggested that death was due to intrauterine asphyxia several hours before the death of the mother.

Due to post-mortem autolysis, histological sections were of no diagnostic value.

Anatomical diagnosis.—Syphilitic aortitis; diffuse petechial hæmorrhages in the brain, with terminal thrombosis and bilateral infarction of the medial part of the temporal lobes; exudative cholangitis; septic splenitis; passive hyperæmia of the lungs; productive pleurisy (bilateral); diffuse petechial hæmorrhages in serous cavities and parenchymatous organs of the fetus.

DIAGNOSIS

The clinical course in this patient suggested a hæmorrhagic encephalitis rather than a Herxheimer reaction in a localized area of cerebrovascular syphilis. The onset of the symptoms was more delayed than is usually seen in a Herxheimer reaction to the trivalent group of arsenicals.[1] Headache and abdominal pain were not present, but the history of fever, disorientation and confusion, followed by convulsions and

coma, strongly suggested the encephalitic type of lesion. This was amply substantiated by the pathological report.

Eclampsia was considered in the differential diagnosis on account of the slightly elevated blood-pressure, and the faint trace of albumin and a few granular casts in the urine. The convulsions, however, were not typical of eclampsia, and this possibility was definitely eliminated by the post-mortem findings.

A very unusual feature of the case was the marked generalized vascular paralysis in the liver, kidneys, spleen and lungs. This is an uncommon finding, since in most instances in which hæmorrhagic encephalitis is the cause of death the lesions are confined to the central nervous system and particularly to the white matter at the base of the brain.[2] The present case was again unusual in that the area of greatest vascular damage was in the grey matter of the temporal lobe. Extra-cranial hæmorrhages have been reported in the pleura and pericardium,[3] and in the liver, spleen, kidneys and lungs.[4]

Some authors[5, 6] have suggested that the capillary damage is initiated by adrenalin insufficiency, which in turn is caused by the toxic action of the arsphenamines on the suprarenal glands. These observations have not been widely confirmed, however, the consensus being that the arsphenamine acts directly on the capillary endothelium in idiosyncratic patients. The present case did not present any demonstrable lesions in the adrenal glands.

The lesions in the liver and spleen were of an unusual type.[5] Superimposed on the arteriolar paralysis was an early parenchymatous necrosis which seemed more extensive than was warranted by the vascular dilatation. Multiple visceral capillary hæmorrhages[4] were not seen. The pathological evidence of liver damage was further substantiated by the blood-chemistry report, which revealed a normal non-protein nitrogen, with a very low urea-nitrogen. It would seem, too, that these lesions were primarily due to arsphenamine idiosyncrasy. The total bismuth given was relatively small in amount, and, in addition, metallic bismuth preparations are said to be absorbed with extreme slowness.[7]

Abnormalities in the spinal fluid suggesting cerebro-vascular syphilis have been reported in a few of the patients dying of hæmorrhagic encephalitis.[3, 8, 18] The spinal fluid, taken from the above patient about ten hours after death revealed a Wassermann reaction of 41000, a slightly increased Pandy and cell count, and a colloidal gold curve of 0000120000. This suggested, of course, cerebro-vascular syphilis, even after discounting the effects of post-mortem autolysis, but endarteritic lesions were not found in the brain. Any that may have been present were certainly not in the area of vascular damage.

DISCUSSION

There has been much speculation as to the exact nature of the vascular accidents following arsphenamine therapy. It may be that the different syndromes are expressions of varying degrees of severity of the same essential process. Transitory vasodilatation results in a nitritoid crisis, while cutaneous purpura is the result of a more prolonged capillary injury. Acute cerebral stasis gives rise to a type of serous apoplexy,[9] and when the stasis is more profound, capillary and even gross hæmorrhages occur. Hæmorrhage without preceding stasis has been reported.[10] The leptomeninges were dry in the present patient. It would seem that the "hyaline" thrombosis in the capillaries[2] represents the end-result of the vascular paralysis with complete stasis. It may be related both to the early capillary dilatation and the locally toxic action of the arsphenamine for the endothelium.

The selective action of arsphenamine on the brain capillaries in young persons has not yet been explained. Visceral hyperæmia[2] is apparently but a minor factor in the final outcome, as is the occasionally reported kidney damage[5, 11, 12] and suprarenal injury.[5, 6]

LITERATURE

The literature was reviewed, to correlate significant known facts concerning the etiology, course and treatment of the syndrome. Fifty-six references were personally consulted, while twenty others, written for the most part before 1920, were not available. The conclusions and trends will be but roughly summarized, since many references did not contain complete data. In addition, many of the cases have obviously gone unrecognized or unreported.

Approximately 135 instances of "hæmorrhagic encephalitis" are reported from arsenic.

The sex was stated in 102 cases. There were 56 males and 46 females. Thirty-four of the 46 females were pregnant! The average age for the group was 22.5 years. The youngest patient was a boy 2 years of age;[13] the oldest, a woman of 48.[14] The relative number of deaths from arsphenamine and neoarsphenamine were about equal, and constituted the great proportion of the cases. Sulpharsphenamine was the responsible drug in 12 instances, a relatively large number when one considers the small total number of patients treated with this drug. For this reason it has been largely discarded by many experienced syphilologists.[15] Its supposed lack of toxicity in children is not entirely borne out by the above reports, since 6 of the 12 cases occurred in young children. Acetarsone was used in one patient.[16]

In the non-pregnant patients age rather than the type of the syphilis present seemed the important factor. About 60 per cent of the patients had early syphilis; the greater proportion of the remainder had latent syphilis. General paralysis was recorded in 2 instances.[14, 17] Two non-syphilitic patients were included, one with Vincent's angina, the other with multiple sclerosis.[18] The characteristic time for the appearance of symptoms was from 50 to 70 hours after the second injection of arsphenamine. In a somewhat smaller number they appeared after the third, fourth and first injections. The earliest appearance of symptoms was one-half hour after the first injection of neoarsphenamine (0.3 g.),[19] the latest, after the thirty-fourth injection.[20]

The treatment was effective in about 10 per cent of the non-pregnant group. The most effective procedures, in the order of their importance, were (1) large and repeated doses of adrenalin, (2) spinal drainage, (3) hypertonic solutions intravenously, (4) sodium thiosulphate.

The group in which pregnancy was present were all young patients, the average age being 21 years. About 25 per cent had early syphilis, the greater portion of the remainder being in the latent phase of the disease. The spinal fluid Wassermann reaction was positive in three patients,[3, 8] one of whom had secondary syphilis. All of the patients were conspicuously healthy. Only one had had a previous reaction, this being an acute urticaria to the preceding (2nd) injection.[21] One other patient who had received two injections of sulpharsphenamine and one of neoarsphenamine developed, simultaneously with the hæmorrhagic encephalitis, an early generalized post-arsphenamine dermatitis.[22]

Hæmorrhagic encephalitis has been described in all but the first two months of pregnancy. The average length of the pregnancy was 5.5 months, suggesting that the date of the beginning of treatment was more significant than the metabolic overload at the end of pregnancy.

Arsphenamine and neoarsphenamine were the drugs used in all but one of the patients, the incidence of the reactions to each being approximately equal. Sulpharsphenamine was used in one case.[22] Dosage estimates revealed a surprising fact. Nearly every patient had received from two to three injections of 0.45 g. of neoarsphenamine (or its equivalent) within a five- to seven-day period, and in some the total amount injected was even larger. This is in striking contrast to a recently reported series of nearly 1,000 pregnant patients[23] treated with neoarsphenamine in a dosage not exceeding 0.3 g. per week. Hæmorrhagic encephalitis did not develop in a single instance!

The yearly incidence of the complication is of interest, twenty-one of the cases being reported prior to 1920, seven between 1920 and 1930, and six after 1930. This coincides roughly with the larger dosage scales used in the earlier years.

Preliminary treatment with heavy metal was given to approximately one-third of the group. It apparently had little if any relation to the development of the hæmorrhagic accident. There was no correlation between the occasionally reported kidney damage and the administration of heavy metal. It was given, in conjunction with the arsphenamine, to as many patients in the early as in the late months of pregnancy.

The reaction, in the majority of cases, developed after the second injection of the arsphenamine, a small number occurring after the first and third injections. One patient had received six injections. The average time of onset of symptoms was 53 hours after the last injection; the average duration, two days. Prodromes were usually present, but in one

case convulsions began without warning. Headache was the most common early symptom, then, listed in the order of their frequency, came fever, head or generalized body pains, dizziness, restlessness, nausea, and vomiting. Signs of focal damage occasionally occurred, but were late in their appearance. In one patient however, a motor aphasia was the first sign of distress.[12] Delirium frequently supervened, although some patients sank directly into a semi-stupor and thence into coma. About 50 per cent had convulsions, which were sometimes focal in type at the onset, but were more apt to be generalized. When present they invariably became generalized.

The blood-pressure was not initially high in a single instance. Urinary changes were slight and were usually terminal in nature. A moderate leucocytosis was frequently observed.

The pathological changes in the brain were usually concentrated in the white substance, although scattered hæmorrhages were often seen in the grey matter. The most frequent sites were the corpus callosum, the caudate and lenticular nuclei, the pons and the medulla.

The essential lesion was a diapedesis of red cells around the dilated capillaries. These were frequently of the ring type, although the solid ball type,[18] resulting from the occlusion of an arteriole and its branches, was often seen. The large areas of hæmorrhage were formed by the coalescence of many smaller capillary lesions. "Hyaline" thrombosis of the capillaries was common. Actual degeneration of the brain tissue was but rarely seen, because of the rapidity of the encephalitic process. Bloody spinal fluid, depending on large hæmorrhagic lesions adjacent to the spinal canal or ventricles, was reported in one patient.[22]

SUMMARY AND CONCLUSIONS

1. A case of arsenical "hæmorrhagic encephalitis" during pregnancy is reported.

2. Significant factors in the causation of the syndrome are analyzed; of these overdosage is the most important.

3. Neoarsphenamine, 0.3 g. weekly, is advocated as the maximum dose to be given in pregnancy.

4. The incidence of "hæmorrhagic encephalitis" is apparently higher in pregnant than in non-pregnant women.

5. Any young patient complaining of headache, abdominal pains, fever, restlessness, or nausea, coming on about two days after any of the first few injections of arsphenamine, should be watched closely to prevent the development of a possible "hæmorrhagic encephalitis". Adrenalin should be given in large dosage, and spinal drainage done if signs of cerebral œdema are present.

The author wishes to express his thanks to Dr. W. H. Chase, of the Pathological Institute, for the interpretation of the pathological findings.

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THE EFFECT OF ŒSTROGENIC HORMONES ON THE NASAL MUCOSA; THEIR ROLE IN THE NASO-SEXUAL RELATIONSHIP; AND THEIR SIGNIFICANCE IN CLINICAL RHINOLOGY*

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THE belief that changes occur in the nose in association with certain sexual happenings dates from antiquity, and doubtless its basis has been largely the obvious relationship between the sexual and nasal functions in the lower animals, and the sexual stimulation associated with certain olfactory perceptions in man. It was not, however, until the nineteenth century that the nature of this relationship became a matter of interest and of investigation by physicians. While it is true that Bresgen,[1] in 1881, observed that there is apt to be a generalized congestion of the nasal mucous membrane during menstruation, it is to Mackenzie[2] (1884) that we owe the first accurate observations in this field.

Although he did not give the total number of cases on which his observations were based or the conditions of examination, he stated unequivocally that "in a certain number of women, whose nasal organs are healthy, engorgement of the nasal tissue occurs with unvarying regularity during the menstrual epoch, the swelling of the membrane subsiding with the cessation of the catamenial flow". He was satisfied with the accuracy of this statement by direct inspection of the turbinals, "before, during and after the monthly period". He noted that the conchæ were chiefly involved in the change, that the condition might be poorly marked or, on the other hand, so well developed as to occlude the nostril; that it might be bilateral or unilateral, the change occurring first on one side and later on the other. He noted a case of his own where the engorgement occurred at the expected time of the period, although uterine bleeding did not occur. He raised the question as to whether similar changes might occur in pregnancy, but was himself unable to make any statement in this regard owing to lack of opportunity to investigate this aspect of the question. He concluded that there was "an intimate physiological association between the nasal and reproductive apparatus", which he found explicable partly as a reflex action, and partly by "the bond of union that exists between the various erectile structures", and the inference is that here also he was thinking of a nervous mechanism when he says that "the irritation of the one reacts upon the circulation and, possibly, nutrition of the other".

In 1892 Endriss,[3] in an M.D. thesis, reviewed the literature of that time on the "physiological and pathological relationship between the sex organs and the mouth, nose and larynx". With reference to the nose in its relationship to the sex organs he cited 59 publications covering the period from 1835 to 1891. There are only twelve references prior to 1884. Of these, ten relate to nasal bleeding as vicarious menstruation, as a prodromal symptom of the first menstruation at puberty, as a post-menopausal or as a post-castrational occurrence. Mackenzie's work is the second citation; this occurs in the opening paragraph and would appear to have been this author's starting point or at least an influencing factor in his treatment of this section of the thesis. In addition he cited 5 cases of his own which are of interest; one patient, suffering from ozæna, was worse during menstruation, a fact that had been noted by others, while another with this disease became markedly improved during pregnancy and again worse after delivery. He reported a case of epistaxis in menstruation and, more noteworthy, another in which the nose-bleeding was pre-menstrual in time, ceasing with the onset of the menstrual flow, while the fifth patient showed hyperæmia and swelling with a sensation of burning and blocking in the nose two days before the period, the local appearances disappearing two days after cessation of the flow.

Apparently at this time the literature for the most part dealt with the question of epistaxis in relation to the various aspects of sex function, for 73 per cent of the citations are relative to this subject. Apart from bleeding, the nose might show other symptoms in evidence of the sexual relationship, for example, engorgement and blocking of the nose, excessive or scanty secretion, sneezing attacks, etc., associated with menstruation, pregnancy, coitus and onanism. Also there might be disturbance of olfactory function, such as anosmia after castration and at the menopause, in which latter condition there might also be, as in early pregnancy, olfactory hallucinations. The general view held as to the nasal bleeding was that it was either a result of a general congestive state, the nose standing in some special but non-precise relationship to the sex organs in phylogeny; or that the menstrual flow itself, as well as its vicarious manifestation in the nose, played the rôle of a periodic, constitutional catharsis. The

* Presented in preliminary form by Dr. R. Percy Wright, in the Section of Oto-laryngology, Sixty-seventh Annual Meeting, Canadian Medical Association, Victoria, B.C., June 24, 1936.

other manifestations were apparently held to be produced "reflexly", although the reflex path was more imagined than known.

It becomes clear that it is to Mackenzie that we owe the first recorded observation that there occurs in the nose a periodic engorgement, that it was coincident with the menstrual flow, and he first defined the specific areas in the nose that this engorgement affects. Also, he was the first to indicate that the relationship between the sex organs and the nose might be reciprocal, so that not only might nasal irritation and disease result from affections of the genito-urinary tract, but the converse might also occur. In this last respect he anticipated Fliess in his ideas by several years. This author,[4] in 1897, reported the changes which he found in the nose in menstruation, during pregnancy, at labour and in the puerperium. These changes were hyperæmia and swelling and increased sensitivity in what he called the "genital spots", which at those times had a tendency to bleed. The spots were portions of the middle and lower conchæ and the tuberculum septi. In practice, by local treatment of the spots, he successfully treated certain forms of dysmenorrhœa and controlled to some extent the pains of labour, and on his observations he built his theory of the causation of a certain type of dysmenorrhœa and many associated conditions, a theory which, with its expansions, while it found many supporters, did not fail to find as many critics. From this a large literature on nasal dysmenorrhœa and related problems resulted, the question of the condition of the nose in menstruation, pregnancy, labour and the menopause receiving the attention of a number of authors. The nature of the physiological relationship, as well as the pathological conditions that might result therefrom, was much discussed, so that, in 1912, when Seifert[5] published his outstanding critical study of the whole question, he cited 296 references thereto, three-quarters of those being published between 1900-12, including only 11 that had previously been given by Endriss. The large part of it mainly concerns nasal dysmenorrhœa and its treatment, but from the study of the whole field, Seifert expressed the conservative opinion of that time in the following conclusions.

1. There exists a striking anatomical and physiological correspondence between the sex organs and certain parts of the nose, and many appearances indicate a direct nervous relationship between them, but the path of such nervous communication is not known.

2. General conditions, both circulatory and mechanical, would seem to exert a more or less marked, modifying influence on the objectively perceptible nasal appearances found in association with certain sexual functions and conditions.

3. Numerous pathological conditions may be explained by the supposition of a genuine nasal reflex neurosis or of an already existing nasal condition with its local and general consequences.

4. Fliess' theory and its various developments cannot be accepted. The good results obtained by Fliess in treatment can be explained as operating either by suggestion, by cocaine euphoria, by the removal of the nasal source of affect in the reflex neurosis, which is the cause of the pain in such forms of dysmenorrhœa, or else by the improvement in general health which followed the removal of nasal obstruction.

In these conclusions no mention is made of the possible influence of ovarian or other hormones upon the nasal mucosa, although in the discussion of the various views that had been advanced in explanation of the physiological relationship Seifert did mention the pituitary gland, referring to the known enlargement of the hypophysis in pregnancy, which he imagined might have an effect upon the nose, the possibility of this arising from the effect noted in acromegaly, namely, the enlargement of the nose as a whole in certain cases. To this, however, he did not attach much importance, confessing himself more impressed by the possibility of an ovarian influence, but concluding that "it is too early and too risky to explain the naso-genital relationship by hormone effects". In 1904 Freund[6] had observed nasal changes in pregnancy, and his view was that the nose participated with other organs, such as the thyroid, in an enlargement that was due to the circulatory changes induced by the activity of the corpus luteum.

Since 1912 the literature on the naso-genital relationship has been slight, and for the most part consists of case reports of nasal dysmenorrhœa, vicarious bleeding from the nose, etc. It would appear that the nasal treatment of dysmenorrhœa is much less in vogue today, and that the nature of the physiological relationship between the sex organs and the nose has become a problem of diminished interest.

Recently, we have had an opportunity of reopening this question, and were able to show that in the female monkey (*Macaca mulatta*) the mucous membrane of the conchæ responds specifically to the administration of œstrogenic

hormones.[7] It may not be obvious at first that the female monkey as a test object in such an investigation is superior to the human female. Anatomically and histologically, the monkey's nasal cavities closely resemble the human, with the exception that in the monkey the so-called superior concha and the concha suprema, found in man are not present, the upper concha of the monkey is homologous with the human middle concha, and we have become accustomed to speak of it as the "middle" concha.

In the course of this work we came to realize that the nasal mucosa in the monkey is much less labile than in man. Acute rhinitis, even of moderate degree, which has always to be taken into account in examining the human nose, is relatively infrequent, and chronic nasal pathological conditions rare. But the great advantage in the monkey lies in the fact that in all save the very immature, in the female, the sexual cycle is very clearly marked by hyperæmia and swelling of the sex-skin, whether menstrual bleeding takes place or not. These changes are dependent on ovarian function. Such changes are not limited to the sex-skin of the perinæum, but are also apparent in the skin of the face, in the nipple, and, as we have shown,[7] in the conchal mucosa of the normal animal; the skin of the back may also react by swelling.[8] In the human female, when menstruation is very irregular, or when amenorrhœa is present, the cycle may be hard or impossible to determine exactly, although the women's subjective feelings may be of aid. Also, in the case of the woman, if she has been previously examined, her individual peculiarities cannot be ignored, for to the appraisal of her condition will be attached involuntarily in the mind of the examiner, to a greater or less degree, the picture observed when she was previously seen. This fact operates to the detriment of even the most sincere attempt to keep the observation objective, and we should like to stress the fact that there exists no record that we know of in which the condition of the nose relative to menstruation was investigated for several months in the same cases where the menstrual cycle of the patients was concealed from the rhinologists until the investigation was completed. We feel that the knowledge of the stage of the cycle when the nose is being examined definitely impairs the validity of the experimental conditions. On the other hand, in a mixed colony of monkeys, where there are more than a score of animals being regularly examined, some of whom are castrates, it is almost impossible, from facial appearance, etc., to become aware of the monkey's identity, of its sex, or whether it is a castrate or not, or to be certain of its stage in the sex cycle, far less to remember the appearance its nasal mucosa presented a week previously.

To render the investigation as objective as possible, three observers, one a professional rhinologist, examined the noses of 28 monkeys weekly for a period of four to ten months. The only information furnished them was the monkey's serial number. Two other trained observers examined the perinæum, face, nipple, and back three times a week and recorded the occurrence of vaginal bleeding; this was done over the whole period of the experiment. Their findings were not disclosed to the nasal examiners except at three to four monthly intervals, when the latter had already charted their nasal findings. Thereupon the condition of the various sex-skin areas was added to the nasal graph on one-year paper, and from the coincidence with variations in the other sex-skin areas, the significance of which is already known, changes in nasal appearance could be seen to assume a clear meaning. Record was kept of both indoor and outdoor temperatures on the dates of examination, and whether each animal had access to the outdoors or not. We were surprised to find that even marked variations in temperature in winter did not correlate with changes in mucosal condition to any extent, and we were able to infer the characteristics of the monkey's nasal condition that we have mentioned above. In the preliminary study, 14 animals were treated, the others being observed under the same conditions. Which animals were under treatment was not disclosed to the nasal examiners.

In view of the recognized variation in colour of the conchal mucosa in the monkey, not only from one animal to another but also in the same animal from one time to another, we represent normality not as a line but as a zone, whose upper limit is marked R, indicating the bright healthy colour of the adult animal, and the lower limit of which is marked P, indicating the pale colour seen in animals in poor condition. The point midway between those, which is marked O, represents a mucosa which clearly appears "normal" in appearance. The effect

of the administration of œstrogenic hormones on the nasal mucosa can be briefly summarized.

1. Crystalline œstrone and œstriol and emmenin cause redness and swelling similar to, and, for the most part, synchronous with, changes already known to occur in other sex-skin areas.

2. This effect can be obtained with œstrone and œstriol in castrated animals.

3. It can be produced in males as well as females, in immature as well as mature animals. Emmenin by mouth enhances what we describe as the normal pre-menstrual nasal peak—makes more evident the nasal evidence of sexual cyclicity.

4. Such peaks acquire clear significance when the average time between their occurrence is observed. In seven animals so treated the average interpeak interval was found to be twenty-six and a half days.

In the untreated control animals, examined for 5 to 10 months, the findings were unexpectedly interesting. There occur in both the mature and immature animals nasal activity peaks which are unrelated to temperature or incidental infection, which are synchronous with peaks of activity in other sex-skin areas, and which occur with even greater regularity than menstrual bleeding. They are in the main clearly premenstrual in time, especially in the immature animal in which vaginal bleeding may not be a very regular occurrence, although it is already obviously sexually cyclic. On the authority of our findings in the monkey we thought it advisable to carry out observations both on the nose of normal women throughout the menstrual cycle and in women during pregnancy and the puerperium.

With reference to the former we have under observation, at the present moment, 25 young nulliparous women who are both normal in their nasal mucosa and who do not suffer from disturbance of menstrual function. The observations on them will be the subject of a later report. Several authors have examined the nose during pregnancy. As already mentioned, Mackenzie lacked the opportunity of doing this, and the first record is made by Fliess[4] who, although he did not state the number of cases observed, drew from his clinical experience the following conclusions.

1. That during pregnancy a periodic occurrence of the appearances characteristic of menstruation was to be seen, and that this appears exactly at the time when the menstrual bleeding would have been expected. This condition was observable also at labour, and, in addition, with the onset of each labour pain, there could be seen an engorgement of the genital spots. After delivery the nasal hypertrophy and hyperæmia gradually disappeared, varying in different cases, but on the whole it could be said that the nasal condition had returned to normal by the time the lying-in-period was over. He also observed that bleeding was frequent during the state of engorgement, but he made no statement as to the percentage occurrence of this manifestation.

Freund,[6] from the examination of 105 pregnant women, came to the conclusion that in about 66 per cent hypertrophy and hyperæmia occurred, especially of the lower conchæ and less frequently of the middle; secondly, that the pregnancy changes in the nose are not periodic but continuous; thirdly, that clinically they were indicated by epistaxis in 25 per cent of cases; fourthly, that such changes are produced by the blood and circulatory apparatus. During the labour pains he found a marked swelling of the conchæ, and he observed that the nasal pregnancy changes often continue during the puerperium, but that the stimulus applied to the nipple by suckling is without influence on the conchæ.

Zacharias[9] obtained similar results, and found in 85 per cent of a series of 100 women that both hyperæmia and hypertrophy occurred in pregnancy. In 22 per cent of the cases, nose-bleeding occurred. He confirmed Freund, but disagreed with both Freund and Fliess, both of whom had observed swelling of the conchæ to a more marked extent, either prior to or coincident with the onset of each labour pain, since of the 34 women in whom he had performed rhinoscopy during labour in 10 only could he observe slight swelling during the pain, and never before its onset.

Oppikofer[10] also examined 100 pregnant women in various months of pregnancy, but, as usually happens in such a series, most of them were at the end of pregnancy. He did not find a single case in which the changes that he observed could be referred with any certainty to pregnancy. He admits, however, that he did find hyperæmia here and there, but always in the history he found evidence of acute catarrh. Only 6 of his cases suffered from nose-bleeding, and he makes the admission that on 26 occasions, or in every fourth woman, he found hypertrophy of the mucosa of one or other of the conchæ. Further, he never observed changes after delivery, although he subsequently admits he saw swelling at the beginning of labour, and that after delivery the mucous membrane was usually a little paler. He also examined 50 menstruating women, and here again he reports his findings as largely negative. Seifert[5] examined 56 cases in pregnancy, at labour, and during the puerperium. Only in 7 did he fail to find changes, during delivery and for a short time after. During the last weeks and days of pregnancy he observed, in the majority of them, an increasing swelling of the lower conchæ and, less frequently, of the middle also, but very seldom at the tuberculum septi. They often showed marked redness; sometimes, however, they were only swollen and pale, with a glossy appearance. He could not confirm the periodic character of the changes with Fliess had described. Although he looked carefully for acute swelling during the labour pains, he never observed it. He found epistaxis not infrequently, and on examining such noses he found evidence of its coming from Kiesselbach's triangle.

In view of these contradictory reports, it was necessary for us to investigate the nose in pregnancy and, to date, we have been able to examine 60 pregnant women at the Prenatal Clinic at the Montreal General Hospital. Only patients giving a negative nasal history were

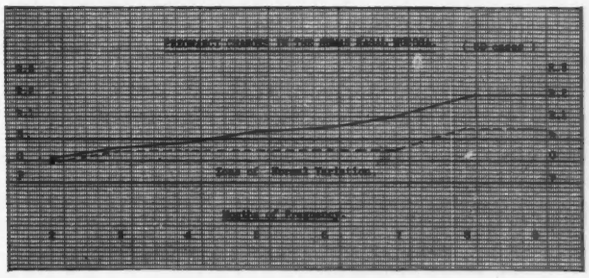
examined and, in those, any found to suffer from such conditions as unsuspected hypertrophic or atrophic rhinitis or chronic infection of the accessory sinuses were rejected. Although the survey is not completed and is to be continued for at least another year, we feel justified in offering for preliminary consideration the results thus far obtained.

Of the 60 pregnant women examined, 31 were only seen once during pregnancy, with naturally more than half of them (17 cases) from the 7th month onwards. In these last all but one showed an abnormal redness and swelling of the conchæ; 2, seen in the second month, had normal noses, and it is obvious, when these 31 cases are taken as 1 case, running from the 2nd to the 9th month, that definitely abnormal redness and swelling appeared in this group somewhere about the 4th month, and increased gradually, reaching its maximum at the 9th.

Seven women were seen twice in pregnancy, not, however, in consecutive months. Charting them as single observations, the average condition shows normal or only slightly high coloration at the 4th to 5th month, with increasing redness and swelling in the 6th, 7th and 8th months. Fourteen women were observed for 2 consecutive months. They show the change as early as the 4th month and a similar increase as pregnancy advances. Six were observed for 3 consecutive months, 4 being first seen at the 6th month and 2 at the 7th. Two were within normal limits at the 6th month, one of whom rose in the 7th and 8th, while the other showed no change in colour at all with only one-half a degree of swelling in the 8th month. The latter was an unmarried mental-deficient in poor physical state. The remainder all showed increase in colour and swelling as pregnancy advanced.

One woman was examined for 4 consecutive months, beginning at the 6th, when she already showed well marked redness and swelling, which increased with the progress of pregnancy.

By striking an average of the changes, month by month, in the four groups just discussed a grand average is arrived at, which gives (Graph 1) the following indication of the progressive changes in the nasal mucosa of the pregnant human female. Taking the zone R to P as that of normal variation in colour and activity of the mucosa, it is apparent that in the second month of pregnancy the nose is entirely normal. By the end of the 3rd month there is a tendency for a slight increase both in colour and activity, still, however, within normal limits. By the end of the 4th month the top limit of normal coloration has been reached, but swelling is not a marked feature. By the end of the 5th month the colour is slightly above normal limits, while at the end of the 6th, it is somewhat higher, and at the 7th it is unmistakably higher. It is not, however, until



GRAPH 1

the 8th month that all the cases, with one exception, showed an almost maximal redness, which is sustained until delivery. Swelling is not as a rule a marked feature, or one of which one can be very sure, until the end of the 7th month, and thereafter it is usually a well marked feature, so that the average is above normal.

With Dr. George Hilton, of the Oto-laryngological staff of the Montreal General Hospital, we made a clinical examination of the patients, and observed that this nasal change found to accompany pregnancy can be distinguished from the appearances produced by rhinitis by the following facts. In pregnancy engorgement the œdema appears more "passive". The mucosa is much drier looking. It has a dull quality. In the acute stage of rhinitis the colour is definitely more brilliant, and in the later stages, when colour becomes dull and the mucosa more "boggy", confusion is not so likely to arise, owing to the presence, usually, of a mucoid or muco-purulent discharge. In addition, in rhinitis, the œdema over the turbinal is much more evident and there is more turgescence. In the later stages the œdema is less pronounced, and as a rule the colour rises.

Fifty per cent of this series showed epistaxis

during pregnancy. Owing to the fact that the greatest number of cases were seen in the last three months of pregnancy, no conclusions can be drawn except that half the women at some time or another showed epistaxis varying in severity, from small particles of blood on blowing the nose to well marked bleeding. It may occur as early as the 3rd month (1 case). On examination small particles of blood clot were observed upon both the middle and inferior conchæ. It is suggested that this may have some significance in view of the fact that, in the great majority of ordinary cases of epistaxis, the bleeding comes from the anterior surface of the septal wall, from what is known as Kiesselbach's triangle. It is of interest to note that the general form of the graph representing the nasal change in pregnancy corresponds closely with what is known to be that of the excretion of œstrin during pregnancy, as has been shown by Browne and others.[11]

It thus becomes apparent that the hormones of the ovary exercise a specific, physiological influence upon the mucous membrane of the conchæ, both during the menstrual cycle in the monkey, and in pregnancy in the human subject. Histological study shows, experimentally, in the former that the nature of this change is a hyperæmia followed by a perivascular œdema in the submucosa. When this is excessive it leads to cellular infiltration, and permanent enlargement of the conchæ may result.

These are facts of paramount importance to the rhinologist in his conception of the etiology of nasal diseases. Leaving aside for the moment the fact that similar changes and results can undoubtedly be produced by chronic infection, the possible influence of the ovary in such conditions as hypertrophic rhinitis and atrophic rhinitis cannot be disregarded. . Even in such questions as individual susceptibility or resistance to the common cold, as well as in a tendency to the manifestations of allergic states, appearing in a person who has never shown such manifestations before, there may be an indication of the gradual effect of hormone disturbance, in the sexual sphere, making itself felt in local nasal changes.

We became interested in this problem from the study of a French Canadian family in whom both parents and all nine children, of whom seven were female, suffered from atrophic rhinitis. The four youngest children had marked ozæna. In the cranial skiagrams no member of the family presented a normal skull; the eldest son showed well marked acromegalic change, while the two youngest girls showed pituitary dwarfism. In four female members of the family, ranging from 11 to 20 years, all showed in the crania evidence of early hypopituitarism, two of them suffering from amenorrhœa. In a moderately large series of cases of atrophic rhinitis we have found this feature in the cranium in 80 per cent, and have come to the conclusion that the constitutional factor in this disease may be related to disturbance of pituitary function, either as a familial characteristic or in the affected individual alone. Since the possibility arises that the anterior pituitary may exercise an effect on the nose, either directly in its control of facial differentiation or possibly through the gonad by its gonadotropic action, it was decided first to investigate the effect of crystalline œstrogenic hormones on the nasal mucosa of a primate, as reported above. After several months of the experiment, during which time it became increasingly evident that œstrogenic hormones possessed a specific effect on the conchæ of primates, producing a vascular engorgement and swelling, we thought it warrantable to apply œstrin in corn oil locally to the conchæ of patients, in the hope that it would thereby induce a physiological hyperæmia that would tend to check the pathological process present. Two of the above female patients have been treated with weekly applications for the past six months, while, without their knowledge, other two receive applications of oil containing no œstrin. One of us (R.P.W.) has inspected the four noses weekly, and has noted not only a very marked improvement, with disappearance of crusting in the œstrin-treated cases, but also a very marked difference in condition between the treated patients and the "controls". We feel, therefore, that mention of this is justifiable at this time, although we are only too aware that much clinical trial will have to be made of this treatment before it can be accepted, and that the two cases reported are inadequate upon which to base a final opinion. A detailed report upon this family and upon the evidences of dyspituitarism in our series of 80 cases of atrophic rhinitis is at present in preparation.

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HEPARIN AND VASCULAR OCCLUSION

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HOWELL has recently reviewed the evidence on the part played by heparin, which was discovered in his laboratory in 1916, in the coagulation of the blood. The work on this anticoagulant in this University was initiated by one of us (C.H.B.) in 1929 with two objectives in view. It was hoped, first, that larger amounts of more highly purified heparin could be made available for physiological work, and, secondly, that the influence of this material on the vascular occlusion resulting from damage to blood vessels might be determined. Our colleagues, Dr. Arthur Charles and Dr. D. A. Scott, undertook the problem of the purification of heparin in the Connaught Laboratories and they have made several reports on this subject. As a result of their work we have had available adequate amounts of purified heparin.

The influence of heparin in the prevention of the occlusion of traumatized veins in dogs has now been demonstrated, and the evidence indicates, first, that no occlusion occurs while heparin is being injected, and, secondly, if the administration of heparin is continued for a sufficient length of time healing of the intima takes place and there is a greatly reduced tendency for the vessel to occlude when heparin injection is discontinued. Heparin also effectively prevents the vascular occlusion which follows the administration of sodium ricinoleate, a chemical used to secure occlusion of varicose veins in human patients. Evidence on the time of administration of heparin necessary to secure healing of the intima damaged by this chemical is being secured.

We have always administered heparin intravenously, but the technique of injection has varied in different experiments. If it is desired, a stream of heparin may be made to flow almost directly on the damaged area (local heparinization). Heparin may be injected intra-arterially in an extremity at such a rate that the blood flowing through the limb is definitely affected, while much less effect on the blood as a whole is produced (regional heparinization). The above remarks, however, on the effects of heparin refer only to the results of *general heparinization*. To secure this general effect heparin is injected intravenously and the blood throughout the body is rendered incoagulable to a degree which depends on the amount of heparin injected.

While the cruder preparations of heparin had definite toxic effects in dogs the more highly purified material (70 units per mg.) has produced remarkably little disturbance in this or in other species of laboratory animals. While the relationship of coagulation of blood to thrombus formation is a vexed question, it will be abundantly apparent that a substance effective in the prevention of vascular occlusion in animals due to mechanical or chemical causes deserves a clinical trial, provided that it can be shown that

We are indebted to Prof. J. G. FitzGerald and Prof. W. E. Gallie for their kind interest in this work. The efficient technical assistance of Mr. Campbell Cowan is gratefully acknowledged.

doses effective in delaying coagulation of the blood have no deleterious results.

The effects of the administration of purified heparin to patients was first studied in the Department of Surgery in May, 1935. A detailed report of clinical experience with this substance will be made in due course. In one patient 4,400 units of heparin were administered intravenously in one dose. The coagulation time of the blood rose rapidly from a normal of 8 minutes to a maximum of 30 minutes, and then slowly returned over a four-hour period to the normal figure. Such a profound decrease in the coagulability of the blood is not necessary to prevent vascular occlusion in animals, and a much less extensive change, secured by the addition of appropriate amounts of heparin to an intravenous injection of saline, has been studied in the more recent clinical trials. No evidence of a negative phase, *i.e.*, a decreased coagulation time after the heparin effect has worn off, has ever been observed in animals or human patients.

This preliminary communication will be followed by a complete report of the results of this work.

MENORRHAGIA AND ITS MODERN TREATMENT*

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MENORRHAGIA—and this old term is as useful and suitable as its more modern variants—is the occurrence of profuse bleeding at the menstrual periods. I am making no effort to define what is meant by "profuse" menses in terms of the actual amount of blood lost. But when one asks a patient about her menses and is told that her period lasts over five days, and that on both the first two days of each menstruation she soils more than five pads or soaks more than three, one is dealing with a menorrhagia, mild or otherwise. Some may object to this rough but practical criterion on the score that it makes menorrhagia very common, but we still adhere to it. Menorrhagia is very common, although not often is it so severe as to induce marked anæmia and prostration.

The pathological basis for profuse menstrual bleeding is commonly an undue hyperplasia of the endometrium, which in turn is due to an excess of œstrin in the blood. Normally, in the first portion of the inter-menstrual interval the endometrium is built up under the influence of this female sex hormone. In patients in whom this endometrium is developed to extraordinary thickness exceptionally large amounts of œstrin are found to be excreted in the urine. Moreover, such hyperplasia has been experimentally induced in both the usual laboratory animals and in the human female by means of large doses of œstrin preparations. So constant has this relationship between endometrial hyperplasia of the so-called Swiss cheese pattern and œstrin excess in the organism proved to be that curettings of this type are now regarded as being diagnostic of such œstrin excess.

Normally, the œstrin phase in the endometrial cycle is followed by the phase of activity of progestin, the principal corpus luteum hormone, and, finally, both the œstrin and progestin are withdrawn or excreted in large part, precipitating the onset of the menstrual flow. This menstruation proper is characterized by a patchy and gradual denudation of the endometrium. Whether it is the decrease of the œstrin or the progestin which actually precipitates the onset of menstruation is as yet uncertain, but the latest opinions seem to be veering over to the idea that it is the withdrawal of the progestin that is responsible. The endometrium is cast off in patches, as has been said, and Traut and Kuder[1] have recently shown how different portions of the same endometrium may be in slightly different phases of maturity at the same time. What largely determines the duration of the menses and the amount of blood lost seems to be the range of variation of this ripe endometrium

* Read at the Annual Meeting of the Ontario Medical Association, London, Ont., on May 29, 1936.

and the thickness of tissue which is to be cast off at the period.

Undue hyperplasia of the endometrium, it has been known for years, may be associated with uterine fibroids or with multiple small ovarian cysts. Witherspoon[2] and others have begun to speculate on the possibility that such conditions in their turn may have been produced by prolonged œstrin stimulation. Whatever the truth of the matter may be, it is certain that these two conditions are among the commonest to be found in association with undue endometrial proliferation.

Other conditions of etiological significance may be mentioned, only to be dismissed with a brief word. Inflammation in the pelvis may make the menses profuse, due to mechanical congestion of the pelvic vessels and their tributaries. Abortion may be followed by profuse hæmorrhage for a time, presumably because abortion is so often accompanied by an excess of œstrogenic substance in the blood, as the author[3, 4, 5] has demonstrated elsewhere. Menorrhagia at the menopause and at puberty seems to depend on hormonal imbalance of much the same type as that discussed in a preceding paragraph. Blood dyscrasias, polypus and cancer are other common causes of menorrhagia. Polypus and cancer appear to produce metrorrhagia as often as menorrhagia. We will discuss anæmia at more length later in this paper.

The major handicap to any proper therapy of these cases of profuse bleeding has been that we lacked an easy laboratory method of blood œstrin determinations. It is true that Frank and Goldberger,[6] with their associates, have done admirable work on œstrin assays of blood samples, and indeed most of our knowledge of the variations of this hormone throughout the menstrual cycle is derived from their researches. However, the method used by them was a biological test, necessitating a considerable number of animals, and even of late[7] they require 15 to 20 c.c. of blood treated according to a fairly complicated biochemical procedure. The other tests in use, such as Cohen and Marrian's[8] modification of the Kober technique, were principally tests done upon urine, and these, unfortunately, by no means indicated the situation in the blood at the same moment.

We have found a new property of blood serum which contains an excess of œstrogenic substance, *viz.*, the power to resist proteolytic digestion by the ferment trypsin for a short period of time. This has been developed by us into a test whose details will not be mentioned here, as they have been thoroughly described recently.[3] Suffice it to say, that one can demonstrate by means of a simple laboratory procedure requiring one and one-half hours whether or not a given sample of 1 c.c. of blood serum contains an excess of œstrogenic substance. We use the term "excess" because our test is not quantitative in any sense, and we have not as yet determined its lower limit of sensitivity. Moreover, the body's content of vitamin E at the moment also determines whether the œstrogenic substance appears as an excess, for vitamin E and this blood œstrogenic substance exist in an equilibrium.[9]

By means of this test we have studied the œstrogenic content of the blood in a series of patients with menorrhagia. These observations have been made at varying times in the menstrual cycle, having regard to the findings of Frank and Goldberger previously mentioned. No statistical analysis of our results will be presented at this time, because statistics are dull at best, and, although they cannot lie, may misrepresent the truth. Suffice it to say that we have found that in this section of Ontario, at least, almost all of these profusely bleeding women show an excess of our œstrogenic substance in the blood just before the period would have occurred normally, on the first day or even later in the period, and at the theoretical mid-interval.

It would seem, therefore, that the desideratum in such cases is a means of excreting more of this œstrogenic substance from the blood. Van Horn[10] and others have shown us how this may be accomplished, for they have proved that moderate thyroid feeding helps to eliminate œstrin, although at the same time it stimulates the gonadotropic hormone of the anterior hypophysis to increase œstrin production in the body. Indeed Van Horn found that it required three times as much œstrin to induce œstrus in rats fed on thyroid as in rats not so fed. Presumably thyroid extract administered to the human female acts similarly to promote the excretion of œstrin. Certainly we have repeatedly found it rendered the bleeding woman's blood free of the excess of œstrogenic substance which

had characterized it before thyroid therapy, and at the same time the profuse hæmorrhage ceased.

Unfortunately, many practitioners have come to rely upon estimations of basal metabolic rate as being a reliable index of thyroid gland function. They have come to place a secondary value upon the clinical signs and symptoms of mild hypothyroidism, for example, because such cases often show no lowering of the basal metabolic rate and do not fit the textbook descriptions of hypothyroidism completely. These textbook pictures are too often the description of severe hypothyroidism or myxœdema. Yet the most profuse menorrhagia can be associated with only a very moderate hypothyroidism, which responds promptly to small doses of thyroid extract. *The most sensitive diagnostic test for hypothyroidism is the reaction of the patient to increasing dosages of thyroid extract or thyroxin.*

How shall we recognize the cases of mild hypothyroidism so frequently associated with an excess of œstrogenic substance in the blood? Perhaps menorrhagia is the commonest and most striking sign, but the patient may have endured it for so long a time that she no longer regards it as abnormal. Constipation of months' or years' duration is another common symptom. Then there may be poor cold tolerance, marked fatigability on very moderate exertion, coarse and dry hair (which "won't hold a wave") and some depilation occurring at the outer ends of the eyebrows. All these signs or symptoms are seldom found in the same individual unless her hypothyroidism has become marked, but none the less hypothyroidism may be suspected if any two, or even one, of these signs or symptoms is present, and then the therapeutic check may be applied.

We commence this thyroid treatment with one-half grain of desiccated thyroid extract each day, and increase or decrease the dose as indicated. Very much less may be required, or as much as three grains each day. We increase the dosage gradually until the symptoms complained of have ceased, or evidences of hyperthyroidism have developed, such as flushing, excessive perspiration, a sensation of increased heat, palpitation of the heart, or insomnia. Then a little less is given than has produced these effects—and that dose again may have seasonal and other variations. We doubt if a transient overdosage does any lasting harm. The treatment may be discontinued after a few months, and its good effects may prove permanent.

Uterine myomata may be present as the cause of menorrhagia or merely as a complication of the etiological factors already discussed. The fibroids may have been present for months or even years before the bleeding began, so that the possibility that they are merely a coincidental finding should always be remembered.

A warning should be uttered against two common modes of therapy of these bleeding women, *viz.*, shotgun prescriptions of hormones, notably those of pregnancy urine or the placenta, and ill-advised surgical procedures designed to correct uterine malposition. Many of the hormone preparations of the day resemble somewhat their demi-monde sisters of the last decade, ovarian tablets. As many physicians and drug houses will be found to recount their effectiveness, and as great a variety of disorders yield to them as if by magic. In order to inculcate a little healthy skepticism it may be useful to recall certain facts.

Extracts of pregnancy urine, and the corresponding placental hormone, were once thought to be able to luteinize ovarian follicles. The persistence of such follicles was associated with the excessive secretion of œstrin into the blood stream, which in its turn produced endometrial hyperplasia and predisposed to menorrhagia. However, the idea that these hormone preparations luteinize ovarian follicles is based on the fact that they do so in rodents, whose corpora lutea develop from the theca cells and not from the granulosa cells of the follicle. In the human female the latter cells are the cells involved, however, and there is little evidence to show that these hormone preparations induce corpus luteum formation in the human ovary, although a rim of theca lutein cells may appear around the follicle. The latest observations on the human ovary,[11] indeed, show that such hormonal preparations produce follicle maturation or even cysts, some follicular degeneration, or thecal luteinization, but no true granulosa cell luteinization. Indeed the author has found that in women in early pregnancy injected with large amounts of a pregnancy urine preparation there is an actual increase of œstrogenic substance in the blood for as long as 42 hours after such injection. Rock[12] and others[13] have found no

endometrial response to pregnancy urine hormone injections that would suggest the production of corpus luteum hormones. In short, it is very difficult to explain the favourable results reported in the therapy of menorrhagia after the use of such preparations by reputable workers,[14, 15] and some recent reports are very discouraging.[16, 17] Perhaps Collip's work[18] may offer some explanation. He pointed out that in monkeys, guinea-pigs and hypophysectomized rats such hormone preparations would produce true corpora lutea in any follicles which happened to be mature at the moment. Or it may be that the formation of even a ring of theca lutein cells in the human ovary has therapeutic value in some types of menorrhagic cases.

It is known, of course, that impure or crude preparations of anterior pituitary have a tendency to produce cystic ovaries. The author recalls seeing such a case in which the ovaries of a young girl which were normal to palpation before treatment was begun were made to increase in size by the administration of such a preparation over a period of a few months until castration was required. At the time of operation the ovaries showed multiple atretic follicles and were about 7 cm. in diameter.

One should say a word about the significance of anæmia in menorrhagia. Gray and Wintrobe[19] have shown that such menorrhagia may improve or may persist during the course of therapy directed only at the anæmia; it may even develop in such treated cases in which the menstrual flow was previously scanty. They conclude: "It has not been our usual experience that menorrhagia, when present, is relieved by iron therapy, as is often stated. In 16 (of their 40) cases menorrhagia continued in spite of the relief of the anæmia."

In an older day, in whose shadow some of us still live, menorrhagia was regarded as fundamentally a surgical problem. It was known that curettage removed the bleeding endometrium, controlled the hæmorrhage, and that sometimes the menorrhagia did not recur. However, the results were usually very temporary and disappointing. Then the surgically-minded physician turned his attention to the uterine corpus which he found was often retroverted, as could be expected. His textbooks told him that the corpus of the uterus was normally anteverted and anteflexed. But they neglected to make quite as much of the fact that in the mature fetus and infant the corpus normally lies in contact with the last lumbar vertebra in an axis approximately the same as that of the trunk, and that this infantile attitude of the uterus often persists into adult years. Forgetting that his first axiom should be *Primum nil nocere*, and remembering only that he must "do something", the surgeon opened the abdomen, was nonplussed by the ease with which the retroverted uterus could be lifted up out of the cul-de-sac, and did what he regarded as his anatomical duty by sewing the organ into a position of anteversion and anteflexion.

Such a sequence of events is to be deprecated. Scarcely any other operation is followed by so many instances of bowel obstruction or by so many recurrences. Many patients date their major abdominal complaints from the time when the surgeon performed this operation for a minor symptom—and failed even in that. A warning against such needless surgery is as timely as a warning against unwise hormone therapy. There is seldom if ever any excuse nowadays for the surgeon who does hysterectomies on women in the 'teens or twenties for menorrhagia. Too many other resources are at his command, palliative measures at least, to justify such emergency treatment. Transfusion will tide the patient over the worst difficulties with or without curettage, and it is noteworthy that in cases in which hormonal therapy is corrective the beneficial effect usually develops inside of a very few days.

Now a word about x-ray and radium. Radiation has little to offer in the emergency treatment of severe hæmorrhages. Approximately one month must elapse before its benefits make themselves felt. Meantime the patient can bleed to death. Moreover, radiation acts primarily upon the ovaries, and its effects upon these are not always predictable. One set of ovaries may be more or less sensitive than another. Some "temporary sterilizing doses" may prove permanent, and others have no discernible effect whatever. There is no doubt that, in young women at least, radiation should be used as cautiously as surgery. There is equally little doubt that it is a tremendous boon in the treatment of menorrhagia due to uterine fibrosis or fibroids in women at or near the menopause. This is especially true if these

women have responded poorly to previous hormonal therapy.

In conclusion, a few case reports are presented.

CASE 1

Mrs. A., aged 27 years, the wife of a physician. Puberty was at the age of 16 years. Since the age of 18 she had had dysmenorrhœa on the first and fourth days of her periods, but a normal menstrual flow. Gradually the dysmenorrhœa increased, until at the age of 21 she was forced to go to bed on the first day and had a profuse flow on the second day of each menses. She married at the age of 23 years. By the age of 24 her dysmenorrhœa had increased in duration, continuing for a week after and beginning some days before the flow, so that only two weeks of each month were free of pain. The pain was worst on the left side, was referred down the whole left lower extremity, and at times as much as three grains of codeine were needed to control the distress. Soon she was taking 50 grains of aspirin each day for as long as six weeks at a time. The menses became quite profuse, lasting six to seven days. Finally on September 8, 1932, she had a left ovarian cyst and chronic appendix removed, and a uterine suspension done.

She no longer had such prolonged distress between menstrual periods nor the pain referred down the leg, but her next menses after the operation were as profuse as before, and she experienced the worst backache to date at that time. The dysmenorrhœa and menorrhagia continued during the summer of 1933, unrelieved by the use of a pessary to restore the position of the uterus (which was no longer "suspended"). By October, 1933, the periods had become very profuse, came every three weeks, and the hæmoglobin had fallen to 65 per cent (Sahli). On intensive iron therapy the hæmoglobin was restored to about normal. The menstruation at the end of November was accompanied by intolerable pains, with such profuse hæmorrhage that she fainted repeatedly while walking about the house, bled through doubled pads repeatedly, and the hæmoglobin fell to 65 per cent again within three days. The basal metabolic rate at this time was +3 per cent on several readings. She was now put on thyroid extract, one-half grain each day, on my advice, and given antuitrin S just before the menses began on the advice of another physician. The most normal period in years ensued. She used only seven pads for the whole menstrual period, and the pain was relieved for approximately 18 hours by each injection of antuitrin S.

This combination treatment was continued for three months with the same result. The antuitrin S was then stopped and she was kept on one-quarter grain of thyroid extract each day. The periods remained normal, with slight pain on the first day only. A pregnancy occurred which ended in a spontaneous abortion. Without thyroid therapy the menses remained normal except for one exacerbation in 1935, promptly controlled by thyroid extract as before. A second pregnancy occurred and nothing of note since.

CASE 2

Mrs. B., aged 30 years, the wife of a physician. She had always had a considerable amount of dysmenorrhœa on the first day of her menstruation, but was regular and normal otherwise until after her first pregnancy. This first pregnancy ended in a spontaneous abortion at six weeks in August, 1933. One profuse period ensued and then she conceived again. At the third month her basal metabolic rate was −21 per cent and her hæmoglobin 65 per cent (Dare). She was accordingly given a preparation of ferrous sulphate, calcium, whole thyroid gland, two grains each day, and for a time three drams of wheat germ oil each day. A normal, full-term delivery occurred in July, 1934.

Following delivery the menses began again and were regular, lasting six to seven days as before, and accompanied by a dysmenorrhœa on the first day, which ceased as the flow began. The menses were alternately scanty and normal, but rapidly became more profuse, until one was approximately normal and the alternate one very heavy. The greatest flow occurred on the third day each time. In February, 1936, the basal metabolic reading was −12 per cent and the hæmoglobin 75 per cent (Dare). No therapy but erneutin had been attempted for the menorrhagia up to this time. No curettage had been done. Pelvic examination had revealed no abnormality. However, in February she was put upon thyroid extract (desiccated, P.D. & Co.), one-half grain each day, increased to one grain in the week prior to the onset of menstruation. Since then the menses have been normal and the dysmenorrhœa reduced to a negligible amount.

CASE 3

Mrs. C., aged 28 years, was first seen on January 25, 1935. She had had mumps during her first pregnancy in 1929 and a transient glycosuria. A second pregnancy shortly afterward ended in a spontaneous abortion at three months, followed by a curettage. Ten months later, in November, 1931, she was delivered of female twins after a mild late toxæmia of pregnancy. The twins were weaned when two months old, and six weeks later she menstruated. She then moved from New York to London, and this was followed by an amenorrhœa for two months. A physician gave her some pills to start her menses, and she had never stopped bleeding from the vagina since for more than two or three days at a time until she consulted the author. During 1934 she passed clots with her hæmorrhages and had begun to feel very weak.

There was a history of very poor tolerance of cold, defective perspiration in hot weather, stammering, nervousness, and mild constipation. Her skin was very dry and rough. The thyroid gland was normally palpable. There was a dermatitis of the scalp and right forearm. Pelvic examination revealed no abnormality except an old cervical laceration, with a granular appearance of the everted lips. The hæmoglobin was 50 per cent (Sahli).

She was given thyroid extract (P.D. & Co.) one grain twice each day with one ferrocatalytic capsule (Frosst) three times each day. On February 1st she reported a much scantier menstrual flow, but still required to wear a pad constantly because of some slight metrorrhagia. The dosage of thyroid was raised to one grain three times each day. The metrorrhagia ceased at once, the skin was greatly improved, and the dermatitis disappeared. She complained of feeling drowsy, however. Her dosage was reduced to two and a half grains each day. The menstrual period on March 1st was normal in amount, but a slight spotting of blood ensued for another seven days. She felt much more energetic.

She was seen again in September, 1935. She had lost no weight, was taking between three and four grains of thyroid each day, and had had regular normal menses since she was last seen. Her skin was of normal texture. There had been some sleeplessness at night, however. Her thyroid was stopped entirely and she has since remained well.

CASE 4

Miss D., aged 17 years, was first seen on January 27, 1936. Puberty, at the age of 14 years, had been followed by profuse menses which had increased steadily during the past year. She thoroughly soaked at least six or more pads on each of the first two days of her period, and she might bleed even through these. The menses lasted about six days and occurred at 28-day intervals. She had been constipated for years, and this, too, had lately increased. This was accompanied by

much flatulence and belching and even borborygmus. She was nervous and irritable, unduly fatigued by her easy work, and her skin was always dry. Her appetite was excellent, and there was no deficiency of cold tolerance. In summer she perspired freely. The thyroid gland was scarcely palpable. There was some abdominal tympanites. The cæcum, ascending, descending, and sigmoid colon were palpable and slightly tender throughout almost their entire length. The reflexes were sluggish. Pelvic examination revealed an intact hymen. A rectal examination revealed nothing but a uterus slightly enlarged for her age and soft. Her hæmoglobin was 78 per cent (Sahli).

She was given one-half grain of thyroid extract (P.D. & Co.) each day. On February 7th, her menses began and were less profuse. She noticed less constipation. Her dose of thyroid was increased accordingly to one grain per day. She developed a decreased cold tolerance on this regimen but her constipation ceased. On March 6th she menstruated again, and she used three pads on each of the first two days, had a scanty third day, and nothing more. Curiously, however, she was "shivering with the cold all the time" in weather much warmer than when she first was seen. She had also become extremely fatigable. Accordingly, her dosage of thyroid was cut to one-half grain per day. The April period was too scanty (she used only two pads each day for three days and they were merely soiled). A slight tachycardia was present, as well as some sleeplessness, and increased nervousness. Therefore she is now being carried along on one-quarter grain per day. Her menses are normal, and she seems normal in every other respect.

CASE 5

Mrs. E., aged 26 years, was first seen by me on February 8, 1934. At that time she was five months pregnant, was an obvious case of endocrine dysfunction, weighed about 236 pounds, and had a history of familial epilepsy. She had married at the age of 17 years, had become pregnant within two months, had delivered a Mongolian idiot, and amenorrhœa had ensued for the next seven years. She delivered her child at term normally, and the post-partum pelvic examination revealed no adnexal pathological change.

On January 27, 1935, she began to have an enormously profuse menstruation, for which she was packed and put to bed and given three grains of thyroid extract in a single dose, followed by one grain twice each day for a week. She bled through the pack, but the flow decreased on the 28th and soon ceased. She was then taken off thyroid. There was an amenorrhœa then for five months, followed by normal, regular menses for eight months. She developed intractable and agonizing headaches. In January, 1936, a laparotomy for a subacute intestinal obstruction due to old appendectomy adhesions was done. In March her basal metabolic rate was −26 per cent, and she was put on thyroid extract one grain per day again, but the March period was very profuse for seven days. Her dose of thyroid was increased to one and one-half grains per day. Her weight during the course of the next month fell from 225 to 210 pounds and she felt much better generally and more energetic. Her headaches disappeared and have not recurred. Her constipation ceased and her menses became normal in duration and amount, lasting three to four days. They have been normal up to the present time, and her weight is now 207 pounds.

SUMMARY

1. The importance of excess of œstrin in the blood in producing endometrial hyperplasia is stressed.

2. The author's test for œstrogenic substance in the blood reveals that many cases of menorrhagia show an excess of this substance in the blood.

3. As this indicates the line which therapy should follow, namely, the elimination of such œstrogenic hormone by means of thyroid feeding, the test is of diagnostic significance.

4. The recognition of mild cases of hypothyroidism is stressed, the response to thyroid feeding being the major criterion.

5. The use of extracts of pregnancy urine and placenta in the treatment of menorrhagia is reviewed critically.

6. The significance of associated anæmia is discussed.

7. Unwise surgery and radiation are criticized.

8. Five representative case histories are submitted.

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SERUM THERAPY*

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DEFINITION.—Serum therapy may be broadly defined as the transference of a specific humoral antibody from an animal known to have a high concentration of this antibody in its blood to another animal which it is desired to endow temporarily with an increased supply of the same antibody. The advantage of so broad a definition is that while it emphasizes the basic principle of serum therapy yet all the proper applications of the term appear to be covered. Thus the antivenins come within its scope; the possible use of a species other than equine as donor or other than human as recipient is not precluded; hyperimmunization of the donor is not made an essential prerequisite; and recognition is given to both the prophylactic and the remedial aspects of serum therapy.

Only certain aspects of the subject can be considered here. The antivenins, for instance, and the applications of serum therapy to veterinary practice will not be discussed. I shall confine my attention to the principles and problems involved in the use of certain specific antitoxic and antibacterial substances obtained from the blood serum of hyperimmunized horses for the prophylaxis and treatment of human infections.

Classification.—Hyperimmunized horse serums are customarily classified into two main groups, *antitoxic* and *antibacterial*. Antitoxic serums, or antitoxins, are prepared from horses which have received a series of injections of a bacterial filtrate containing either crude exotoxin or formalinized exotoxin (toxoid), and are assayed by determination of their specific neutralizing power for the corresponding toxin. The antitoxic serums currently available, with their approximate dates of introduction to the medical profession, neutralize *in vitro* the toxins of the following microorganisms: *C. diphtheriæ* (1890); *Cl. tetani* (1892); *Cl. botulinum* (1897); *Bact. Shigæ* (1904); *Cl. welchii, Cl. septique, Cl. œdematiens* (1918); *S. scarlatinæ* (1924); *Staphylococcus* (1934); (?) *N. meningitidis* (1935).

Antibacterial serums, on the other hand, are prepared from horses which have received a series of injections of a suspension containing either dead or living bacteria, and are assayed in terms of either their agglutinating power against suspensions of the homologous microorganism, or, more satisfactorily, their power to protect a laboratory animal against the lethal effects of a measured dose of this microorganism. Serums of this type were introduced, at the approximate dates shown, for use against the following microorganisms: *B. anthracis* (1895); *N. meningitidis* (1906); *Str. pneumoniæ* (1910).

Other less well-known anti-bacterial serums have been prepared, and their clinical use favourably reported on, against: *Bact. flexneri* (1902); *H. influenzæ* (1911); *Bact. typhosum* (1935); *Br. abortus* (1935).

THE PRINCIPLES OF SERUM THERAPY

The first principle of serum therapy is *specificity*. The antibodies which the patient receives must have a specific effect upon the toxæmia, or the infection, or both, from which he is suffering, or against which it is desired to protect him. This principle clearly pre-supposes *correct diagnosis*. An acute pharyngitis due to staphylococcus will not be benefited by diphtheria antitoxin; nor an acute tuberculous broncho-pneumonia by anti-pneumococcus serum; nor a streptococcal osteomyelitis by staphylococcus antitoxin; nor a meningitis due to *H. influenzæ* (Pfeiffer's bacillus) by anti-meningococcus serum. In those rare instances where laboratory facilities are not available for an immediate attempt to identify the causal microorganism in severe cases of acute pharyngitis simulating diphtheria, of pneumonia, of osteomyelitis, or of cerebrospinal meningitis, it is justifiable to administer, without delay, the serum homologous with the microorganism most commonly responsible for the disease in question. But a certain proportion of failures of serum therapy are traceable to this source of error.

Besides *species* specificity there is *type* specificity. Type I anti-pneumococcus serum, for instance, is useless to a patient with pneumonia due to type II pneumococcus. To take another example, *Cl. botulinum* occurs as two types, A and B, which produce antigenically distinct toxins. A case of botulism due to type A toxin would derive no benefit from antitoxin prepared from *Cl. botulinum* type B. As more is learned of the relationship of antigenic structure to

* Largely based upon an address to the Vancouver Medical Association, on April 7, 1936.

pathogenic effects the importance of type specificity in other varieties of serum therapy may become apparent.

The second principle of serum therapy is *potency*. The desired antibodies must be present in high concentration in the serum, so that they may be given in a minimum amount of alien protein. Satisfactory maintenance of this principle depends upon the acceptance of *units*, the imposition of *standards*, and distribution under *licence*. International units of potency have been proposed and accepted for many of the antitoxic and antibacterial serums already listed. Investigation and control of these units has latterly been conducted by the Committee on Biological Standardization of the Health Organization of the League of Nations. Most of these units involve, officially, determination of the highest dilution of the respective serums which will protect some small laboratory animal (usually guinea-pig or mouse) against a stated number of minimal lethal doses of the corresponding toxin or live culture. Various other accessory methods of determining potency are practised.

The production of high potency serum depends upon the operation of several factors, among which are the following: the selection of suitable horses; the use of a satisfactory antigen; correct volume, time, and route of doses; careful checking of the fluctuations in circulating antibody by frequent trial bleedings of the horse; prompt exsanguination when the blood shows an appropriately high titre of antibody; efficient methods of concentration and refinement. While the aim of every ethical manufacturer of serums is to increase the potency of these products, a definite limitation is set by a regulation which prohibits a content of more than 20 per cent of total solids.

The licensing authorities on the North American Continent are the National Institute of Health, Washington, and the Laboratory of Hygiene, Ottawa (operating under the Department of Pensions and National Health). Connaught Laboratories, the only serum institute in Canada, is licensed to manufacture biological products by both Washington and Ottawa, is subject to inspection by their representatives, and observes the standards they impose. The United States regulations require the potency of every serum to be printed on the outside of the package as well as on the label of the vial. Where no official unit has been accepted, the words "No U.S. standard of potency" must appear.

The third principle of serum therapy is *early administration*. Given a supply of specific, high-potency serum, its efficacy will diminish rapidly with delay before administration until a time is reached in the progress of the disease when no amount of serum, however specific and potent, will exert any apparent beneficial effect. This principle involves prompt diagnosis, knowledge that serum therapy is indicated, and availability of the requisite serum. Clinical acumen and ready laboratory facilities are both essential to promptitude and accuracy in diagnosis of the acute infections. But the distinction between use and abuse of the laboratory needs to be more clearly drawn. There is no more to be said for the habit of deferring all attempt at diagnosis until laboratory reports have been received upon numerous specimens from a patient (some crucial test being often the very one omitted), than for the habit of awakening to the desirability of requesting, for instance, a blood culture, only when the patient is already moribund. Even when the diagnosis has been made early in an acute infection, resort to serum therapy is too often unduly delayed. The doctor may not know there is a specific serum available; or he may decide to hope the patient will get well without serum, until the time arrives when it becomes obvious that there will be no recovery whether serum be used or not. Again, serums are regrettably not as accessible as they might be. They are costly, and although some provincial or municipal governments distribute certain types of serum free, the expense of serum therapy is often regarded as prohibitive. But a greater demand for serums would permit a lower price. In any event, the cost of treating a case with serum is usually considerably less than the fee for an emergency surgical operation, though serum therapy may save lives just as certainly as surgery.

The importance of the principle of early administration arises from the fact that many of the characteristic signs and symptoms of bacterial infections and toxæmias are due to a process akin in certain respects to chemical union between the tissue cells and fluids of the infected animal and toxic substances derived from the

microorganisms concerned. This chemical union must be regarded as to some extent irreversible, although the rate and firmness of the union may vary with the different pathogenic microorganisms. In diphtheria, tetanus, or botulism, the union between cell and toxin appears to be almost completely irreversible; and in these diseases, once symptoms have appeared, resort to serum therapy is founded on the hope that widespread toxin-cell union has not already occurred, and on the assumption that any newly-formed toxin will henceforward be neutralized.

It is interesting to contrast the small amounts of circulating antibody which may suffice to *protect* from an infection with the relatively enormous amounts which may be got into the blood stream to no advantage at a late stage in an established disease. The presence of 1/250 unit or more of diphtheria antitoxin per c.c. of serum generally suffices to ensure protection against the disease; yet a patient given serum late may die despite the presence of 10 units or more of circulating antitoxin per c.c. of serum. A prophylactic dose of 1,500 units of tetanus antitoxin given promptly after exposure to infection will usually protect against the disease, although the titre of circulating tetanus antitoxin acquired as a result of the serum injection averages only about 1/5 unit. But one hundred times this titre of antitoxin induced by late serum therapy may prove ineffectual. The maximum amount of specific circulating antibody developed by a patient making a spontaneous recovery from lobar pneumonia rarely suffices to protect mice against more than 100 lethal doses of homologous pneumococci per c.c. Yet a patient may die despite 1 c.c. of his blood having acquired the property, through intensive but late serum therapy, of protecting mice against 1,000,000 lethal doses of homologous culture. Again, the very small amount of measles antibody which can reach the blood of a measles contact, following injection of 10 c.c. of convalescent serum, almost always suffices to prevent the development of the disease if given during the first five days after exposure, but large amounts of convalescent serum have no apparent effect upon the manifest disease. Examples illustrating the operation of this principle might be multiplied; it is of fundamental importance, but is on the whole ill-appreciated.

Closely related to the third are the fourth and fifth principles of serum therapy, namely, those of *optimal route* and *adequate dosage*. From what has been already stated it follows that once the disease is diagnosed, a decision to resort to serum therapy reached, and a supply of specific serum at hand, the paramount objective is to bring a large quantity of the antibody into as intimate a contact as possible with those parts of the body where extensive cell-toxin union has occurred, in an attempt to break up this union; with those foci where toxin is still being produced, in order that neutralization *in situ* may take place; and with those tissues which have so far resisted the effects of the toxin, with a view to protecting them therefrom. In general this objective is best achieved by the *intravenous* route of administration. Given by this route most of the serum injected is at once distributed throughout the body, and the maximum concentration of circulating antibody is reached shortly after completion of the injection. The delayed absorption of antibody from the muscles is not sufficiently realized. Following an intramuscular injection of a serum, *e.g.*, diphtheria, scarlet fever, or staphylococcus antitoxin, from 48 to 72 hours must elapse before the maximum titre of antibody is detected in the blood stream. In a disease of rapid course this delay may be literally fatal. With few exceptions, all serums should be given intravenously, although this route undoubtedly entails more trouble to the doctor and constitutes a greater reaction hazard to the patient. Meningitis is one exception to this rule. In the serum therapy of meningitis, whether meningococcic, influenzal, pneumococcal, streptococcal or staphylococcal, the intrathecal route must be adopted, since very little antitoxin permeates from the blood stream through the "blood-brain barrier" into the cerebrospinal fluid. Intravenous serum should of course also be given when there is a concomitant septicæmia. There are occasions when direct application of serum to an exposed infected surface would seem to be indicated; as, for instance, in a pneumococcal empyema drainage wound, or a carbuncle. Again, in the *prophylactic* use of serums, the intramuscular route, if resorted to very soon after exposure to infection, usually permits sufficiently rapid absorption to ensure protection. But in general the intravenous

route should be regarded as the ideal route of administration of therapeutic serums.

The principle of *adequate dosage* is self-explanatory, though in actual practice far too seldom observed. The general tendency is to give too little serum, and to this fact many of the failures of serum therapy are undoubtedly due. There is no fixed treatment dose of serum, although direction sheets usually state some figure as a guide. In prophylaxis, a definite dose may be fairly safely recommended, but in treatment each case presents a special problem. The age and general condition of the patient, the type and severity of the infection and toxæmia, the presence of complications, and especially the duration of the illness, and the response to the first doses of serum, must all be taken into consideration. The longer the time since onset, the more serum will be necessary. More must be given by the intramuscular route than by the intravenous route. And it is important to be especially liberal in dosage when there has been a blood stream infection, with multiple foci, as *e.g.*, in staphylococcal septicæmia. In such conditions, the blood stream may become sterile and the patient appear much better so that serum is withheld; the circulating antitoxin is neutralized, excreted, or by some other means diminished in titre; and then, a few days later (this has happened so often) a relapse occurs, and staphylococci reappear in the blood stream. The principle of adequate dosage really involves, in fact, that a high titre of circulating antibodies should be maintained until the infection is well localized, and toxæmia satisfactorily abated.

The sixth and final principle is that of *accessory treatment*. Serum therapy is, in many instances, the last resort of the harassed practitioner. To have recourse to serum when a patient is already moribund is tantamount to the requisition of a miracle. In other instances serum may be given comparatively early in the infection, but is expected to eliminate the disease without any other treatment except for rest in bed, an attractive nurse, and a reasonably digestible diet. In the pyogenic infections particularly pus may be expected to form, and should be considered of favourable portent, provided it can be drained. The letting out and mopping up of pus is, after all, a major function of surgery, but one has been repeatedly surprised to note a reluctance to perform this very important accessory treatment.

DIFFICULTIES IN SERUM THERAPY

Some of the main difficulties militating against successful serum therapy fall under the heading *Complications*. These may occur during the course of any relatively simple infection, even when a satisfactory outcome appears in sight. *Secondary infection* is one such complication which is not uncommonly encountered.

To exemplify, a patient being given staphylococcus antitoxin for severe osteomyelitis and septicæmia, and doing very well, suddenly took a grave turn, and died of streptococcal pericarditis; another, apparently recovering with the help of serum therapy from staphylococcal meningitis, developed a double secondary infection of the meninges with a hæmolytic streptococcus and a diphtheroid bacillus, which proved fatal; yet another, during convalescence from staphylococcal septicæmia, had to have a rib resected for drainage of an abscess, and acquired a pneumococcal empyema.

Full use should be made of the laboratory at all stages of severe infections. The reports obtained add inestimably to the value of case records and are essential to the diagnosis of complications of the foregoing order.

A more common type of complication is explained by the tendency of many pathogenic microorganisms to elect peculiar sites for localization. Abscess formation may occur, for instance, in vital and surgically remote parts of the body, such as the brain, kidneys and lungs; and the therapeutic serums in common use have no power to cause absorption of an abscess. Or infection may settle in foci relatively inaccessible to the blood stream and thus become unamenable to serum therapy. This fact accounts, for instance, for an osteomyelitic focus discharging staphylococcal pus long after a septicæmia may have been overcome; for an ear discharging streptococcal pus for weeks after recovery, with the help of scarlet fever antitoxin, from a severe attack of scarlatina; and for pneumococcal pus continuing to discharge from an empyema drainage tract during convalescence from pneumonia successfully treated with anti-pneumococcus serum. The effect of a high titre of specific circulating antibody upon any focus of infection will depend on the extent to which the blood fluids gain access to that focus.

Reactions constitute another serious difficulty rather frequently encountered in serum therapy. These are of different etiology and character, and may be considered under three main head-

ings, allergic reactions, thermal reactions, and serum sickness.

The *allergic reactions* follow parenteral injection of certain substances peculiar to the horse and highly toxic for certain human beings, which it has not yet proved possible to separate from the desired specific antibodies. Dyspnœa, cyanosis, rapid weak pulse, flushing of the face, pain in the abdomen and in the lumbar or substernal regions, apprehension, and collapse, may all be present in varying degree, and their onset is usually within half an hour of the first injection of serum. In its most severe manifestation the reaction may prove almost immediately fatal; but this acute shock-like form is fortunately rare. In other less severe types of allergic reaction the above syndrome may be complicated by urticaria or an acute asthmatic attack. The treatment is by epinephrine, 0.5 to 1 c.c. of the 1:1,000 solution, given subcutaneously, intramuscularly, or, in severe cases, intravenously. Repeated doses may need to be given. While mild degrees of allergic reaction are no contraindication to further administration of serum, provided they prove controllable by epinephrine, if the more severe types of reaction occur, and particularly when accompanied by urticaria or asthma, no more serum should be given.

Most, though not all, allergic serum reactions may be avoided by doing eye and skin sensitivity tests on every prospective recipient of horse serum. In the *eye,* or ophthalmic, test, a drop or two of normal horse serum, diluted 1 in 10, is placed in the conjunctival sac. A positive reaction is marked by erythema, lachrymation, and reddening of the eye within 20 minutes after instillation. In the *skin,* or intradermal, test, 0.1 c.c. of normal horse serum, diluted 1 in 10, is injected intradermally into the flexor surface of the forearm. A positive reaction will be indicated within 5 to 20 minutes by the formation of an urticarial wheal at the site of injection, surrounded by a zone of erythema which may show irregular, pseudopodia-like extensions.

Positive sensitivity reactions to horse serum may be given by:—

1. Individuals spontaneously sensitive to horse dander. Serum therapy is for such persons very hazardous, and is best avoided.

2. Certain individuals subject to asthma, hay fever, and similar allergic conditions. Even if the sensitivity tests are negative it is advisable in patients of this type to precede the injection of serum by epinephrine, while if the intravenous route is to be used a smaller initial dose than usual is indicated, and the injection must be given with extreme slowness.

3. Those who have had an injection of horse serum within a period of from 7 to 10 days up to a few months previously, or who are still suffering from serum sickness (*vide infra*). Sensitivity to horse serum acquired from previous parenteral administration is not commonly very acute after a few months have elapsed, but the precautions stated in the preceding paragraph should be observed.

4. Occasional cases giving no history of either allergy or a previous injection of serum. The existence of such individuals is sufficient justification for the routine performance of the sensitivity tests.

Desensitization may be attempted in individuals who give a positive eye or skin reaction. No one method is prescribed for this, but in severe cases of sensitivity an initial dose of 1/40 c.c. of the serum to be used may be given subcutaneously. Successive doses should be given by the same route at intervals of 10 to 15 minutes, each dose being double the preceding dose, provided that no undue reaction has occurred in the meantime. When 1 to 2 c.c. is well tolerated by the subcutaneous route intravenous administration may be commenced. The rate should be *very slow.* Anti-pneumococcus serum, for instance, which is usually injected from a syringe directly into the vein, should be given at a rate not faster than 1 c.c. per minute, while other serums are perhaps best given intravenously by a slow continuous drip method, diluted in saline, so that the first 1 c.c. may take one hour or more to give.

While the allergic reaction hazard is greatest when serum is given intravenously, it should be emphasized that severe reactions of this type may occur following the intramuscular or any other route of administration if due precautions be not taken to guard against them.

Thermal or *chill reactions* are not due to allergic sensitivity, as ordinarily understood, but to some factor peculiar to the serum, to the patient, to the disease, or to the interaction of these three variables. Between twenty minutes and one and one-half hours after the first injection of serum a general rigor may occur,

lasting up to one-half an hour, accompanied by cyanosis, dyspnœa, rapid pulse, low blood pressure, and apprehension. The temperature may rise several degrees, and subsequently fall, with profuse sweating. Milder reactions of this type need give rise to no alarm, but, if severe, further serum should be withheld for a few hours. In pneumonia or septicæmic conditions, where the temperature is usually already high, alarming degrees of hyperthermia may result, accompanied by pronounced cyanosis, almost uncountable pulse, delirium, convulsions, and collapse. When this occurs no further serum should be given. In the presence of pre-existing obstruction to the pulmonary circulation, severe myocarditis, or hyperpyrexia, a severe thermal reaction may prove fatal. Liability to thermal reactions is not indicated by tests for serum sensitivity. Certain batches of serum seem more prone to contain the reaction-producing factor than others, but in general concentrated and refined products are less liable than crude serums to produce thermal reactions. Epinephrine has little or no effect upon this type of reaction, and the treatment is symptomatic. Precautions to be taken to minimize their incidence include very slow administration of the serum, warming the serum to the body temperature prior to administration, and the rejection of all serums containing a precipitate.

Serum sickness is a fairly common type of delayed reaction to horse serum, with onset characteristically on the 7th to 10th day after the first injection. Urticaria, (which may be very troublesome for a day or so) joint pains and swelling, generalized glandular enlargement, œdematous foci, with mild fever, are the most common features. Epinephrine and ephedrine may prove useful, but for the most part treatment is symptomatic. The condition is never dangerous and is transitory.

A further difficulty in serum therapy is the *incompleteness of available specific antibodies,* due largely to our present comparative ignorance of the respective parts played by different antigens in the pathology of any one infection. Diphtheria, tetanus, and botulism are examples of true toxæmias; that is, the causal microorganisms have no invasive powers, and all the outstanding signs and symptoms of these diseases appear to be attributable to exotoxins disseminated from a focus of multiplying bacteria. But in septicæmic conditions the problem is not only to neutralize exotoxins but also to destroy circulating microorganisms and to eradicate multiple foci of infection. None of the common antitoxic serums is actively bactericidal, although certain of them specifically neutralize *in vitro* the leucocidins produced by their homologous microorganisms and should therefore promote phagocytosis *in vivo.*

The mechanism of bacterial *invasiveness* is as yet very imperfectly understood, and a concentration of effort upon this problem may be anticipated. But the extent of bacterial invasion of a tissue must be largely determined, on the one hand, by the efficiency of the specific and nonspecific protective forces inherent in that tissue (and both local and general treatment should aim at conserving and stimulating these forces), and, on the other hand, by the ability of the microorganism to elaborate *in vivo* certain invasion-promoting substances, such as leucocidins, fibrinolysins, plasma-coagulases, and the "diffusion factor" to which McClean[1] has recently drawn attention. The dual objective of serum therapy in the septicæmias should therefore be to provide not only the appropriate antitoxins but also the specific ancillary antibodies to those invasion-promoting factors which are antigenic. Recognition of this has led to the practice of immunizing horses in the production of certain antiserums with killed or living bacterial suspensions, as well as with the homologous toxic filtrates. Such serums possess, to some degree, both antitoxic and antibacterial properties.

SPECIAL CONSIDERATIONS

Diphtheria and *tetanus* antitoxins remain important, despite the increasing use of diphtheria toxoid, and the practicability of now evoking active immunity against tetanus by means of tetanus toxoid. Since the work of Anderson *et al.*[2] drew attention to the different types of *C. diphtheriæ,* the possibility has been mooted that *gravis* strains might produce a toxin not wholly neutralizable by the antitoxins currently available, and to this has been ascribed the reported failure of antitoxin therapy in occasional diphtheria epidemics. However, experimental evidence has so far been against this hypothesis.

In the serum therapy of tetanus the importance of exceedingly high dosage has been emphasized within recent years. I am indebted

to my colleague Dr. N. S. Silverthorne, and to the Department of Pædiatrics, University of Toronto, for the following information. During one five-year period the dosage of tetanus antitoxin given (by various routes) in cases of tetanus admitted to the Hospital for Sick Children ranged from 20,000 to 100,000 units per case, and of 15 cases, 13 died. In a second five-year period, in which the dosage per case ranged from 300,000 to 3 million units (given mostly intravenously), of 25 cases only 11 died.

The *gas gangrene antitoxins* have, in civilian life, hardly gained the recognition they merit. Prophylactic administration of gas-gangrene antitoxin at any laparotomy involving the risk of fæcal contamination, and to every case of extensive wounds or lacerations, is sound routine procedure.

The N.Y. 5 strain of hæmolytic streptococcus gives rise to an antitoxin which will neutralize the toxins of most hæmolytic streptococci. The fact that certain licensing arrangements require the product to be called *"scarlet fever antitoxin"* if the strain of hæmolytic streptococcus used in its manufacture be of scarlatinal origin, does not detract from its proved value in some cases of erysipelas, puerperal sepsis, and other types of acute or generalized hæmolytic streptococcal infection.

Staphylococci, once regarded as comparatively harmless and unenterprising pathogens, are now known to be exceedingly versatile in toxigenic capacity. There is every likelihood that rapid production of an exotoxin having a destructive affinity for most cell systems of the body, and of such invasion-promoting substances as leucocidin, plasma-coagulase, fibrinolysin, and diffusion factor, is not confined to *in vitro* conditions. Hence a generalized staphylococcal infection always represents so grave an emergency that every recovery therefrom following specific serum therapy may justifiably be considered as evidence of the value of *staphylococcus antitoxin*.

Five years ago, Ferry, Norton and Steele[3] reported that they had obtained soluble exotoxins in meningococcal filtrates, to whose selective action upon the cerebrospinal nervous systems of certain laboratory animals they ascribed the resulting symptomatology of meningitis. Encouraging results have since been reported, particularly by Hoyne,[4] from intraspinal and intravenous injection of *meningococcus antitoxin* in human cases of meningococcic meningitis. There is rather general dissatisfaction with the results obtained with the currently-available polyvalent anti-meningococcus serums, whose efficacy it is desirable to compare with that of the antitoxic serum over an extensive series of parallel cases.

A valuable summary of the place of serum therapy in *lobar pneumonia* is given in a recent monograph by Lord and Heffron.[5] Serum therapy, under favourable conditions, will greatly reduce the case fatality rate in lobar pneumonia due to types I and II pneumococcus; and these two types are responsible for about 60 per cent of all cases of lobar pneumonia. Widespread adoption of the simple and rapid Neufeld method of typing pneumococci,[6] and manufacture of serums against other than types I and II pneumococcus, should lead to the value of serum therapy in lobar pneumonia becoming everywhere undisputably recognized.

Reports on the place of specific serum therapy in *Flexner-type dysentery* are controversial, but the consensus would seem to be that polyvalent serum is of value when given early and in large doses. My colleague Dr. R. J. Gibbons, of the Connaught Laboratories, has prepared a potent antiserum for *B. dysenteriæ Sonne* which in high dilutions will protect mice against several lethal doses of homologous living microorganisms. But the clinical applications of such a serum are again likely to be limited. Infection with *B. dysenteriæ Sonne* is responsible for one type of the gastro-enteritis of infants[7]; but only when an epidemic of this condition has focussed local attention upon it is serum therapy likely to receive a fair trial. Severe cases of the disease in infants usually die before the etiological agent is identified, while mild cases make a spontaneous recovery.

The so-called *influenzal meningitis* (meningitis due to *H. influenzæ*, or Pfeiffer's bacillus) is almost always fatal. The symptomatology of the disease has been carefully described by Neal, Jackson and Appelbaum,[8] who reported a few recoveries following intraspinal and intravenous administration of a specific anti-bacterial serum prepared by immunizing horses with live suspensions of *H. influenzæ* isolated from fatal cases of the disease. Wright[9] has recently recorded a case in which *H. influenzæ* antiserum was used with conspicuous success.

By immunizing horses with cultures of *Bact. typhosum* containing the so-called Vi (virulence) and O (somatic) antigens, Felix[10] obtained serums with a high content of Vi and O antibodies. Animal experiments indicated that the Vi antibody helps to protect against infection with virulent strains of *Bact. typhosum* by suppressing their multiplication *in vivo*, while the O antibody neutralizes the bacterial endotoxin. Administration of the serum to a group of patients gravely ill with typhoid fever was of pronounced benefit, the toxic symptoms in particular being greatly alleviated.

Promising results have been briefly recorded by Mitchell, Humphreys, and Walker[11] from treatment of a small group of human cases of undulant fever with an *anti-abortus serum* prepared by immunizing horses with viable cultures of *Br. abortus*. Undulant fever is probably more common in Canada than is generally realized, and in the acute form is a serious and alarming disease. As laboratory diagnostic facilities improve and the practitioner becomes more familiar with the clinical signs and symptoms of undulant fever the place of specific antiserums in treatment should be extensively investigated.

SUMMARY

1. Success in serum therapy is dependent upon the observance of certain basic principles, among which the following have been illustrated and emphasized: species and type specificity, potency, early administration, optimal route, adequate dosage, and accessory treatment.

2. Special difficulties encountered in serum therapy have been considered under the following headings: complications (secondary infection, inaccessibility of infected foci), reactions (allergic, thermal, and serum sickness); and the incompleteness of available antibodies.

3. A few controversial points relating to some of the well-established serums have been briefly discussed, and reference has been made to certain recently-prepared antiserums which have given promising results.

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CORONARY ARTERY DISEASE IN WOMEN.—Levy and Boas state that in women, especially those under the age of 50, coronary artery disease is unusual in the absence of diabetes or hypertension. Yet precordial pain simulating angina pectoris is a common symptom. Although experienced clinicians have been aware of this fact for years, it is overlooked again and again in daily practice and many mistaken diagnoses result. During the last seven years in an office practice representing largely patients referred for cardiovascular diagnosis, the authors have seen 1,672 women, 169 of whom had coronary artery disease. In the same period they saw 2,135 men, 1,059 of whom had coronary artery disease. The frequency is 4.9 times as great in men as in women. Of the 169 cases in women, 125 were associated with hypertension alone, 25 with both diabetes and hypertension, and 6 with diabetes alone. In only 13 cases was there neither hypertension nor diabetes, and of these only 5 were in women under the age of 50. The clinical picture of true coronary artery disease as it occurs in women does not differ from the generally recognized form. The relative unusualness of conorary artery disease and the frequency of benign precordial pain in women should lead to great caution in the diagnosis of coronary artery disease in women in the absence of hypertension or diabetes. This applies as well to many women in the fifth decade of life with unstable blood pressures and transient rises to 160 or 170 millimeters of mercury. Even in the presence of hypertension in women, true angina pectoris is much less frequent than is benign precordial pain. However, coronary artery disease does occur at times in women with normal blood pressures who are free from diabetes, particularly in women over the age of 60 who have generalized arteriosclerosis. Isolated cases in young women in the absence of both hypertension and diabetes have been reported. Averbuck has pointed out that "when the clinical picture suggesting coronary artery thrombosis occurs in a female patient who has neither arterial hypertension nor diabetes, a pulmonary embolus should be suspected". Hypertension is not the cause of coronary disease but simply accelerates its development. The designation "hypertensive cardiovascular disease", so commonly employed to describe these disease states, is a poor term. It assumes a necessary and fundamental connection between the two disorders. Their true nature can best be discovered by studying uncomplicated coronary artery disease in men and uncomplicated arterial hypertension in women. These apparently represent "pure forms" of these two conditions.—*J. Am. M. Ass.*, 1936, **107**: 97.

ON SOME OF THE NEWER DRUGS

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Coramine

CORAMINE, a solution of the diethyl amide of pyridine beta-carbamic acid, was the result of a research undertaken by Faust to try to prepare a synthetic substance having the pharmacological properties of camphor, so soluble that its pharmacological action could readily be displayed. Camphor has long had a vogue, particularly in Germany, as a cardiac and respiratory stimulant.

The early pharmacological and clinical studies, which appeared in 1924, stressed unduly its effect on circulation and not that on respiration. Further, the dose recommended by the Ciba Company, which still appears on the bottles, is unduly small if respiratory stimulation is to be maintained. These two factors led to a great delay in the recognition of the true importance of the drug, and it was not till the work of Killian and Uhlmann appeared in 1931 that its real usefulness came to be realized.

Respiration.—When the respiratory centre is depressed, either as the result of poisoning of the centre by drugs or disease, coramine is the best drug to use as a respiratory stimulant, if judged by its effectiveness and safety. Herein lies its chief importance. But if the centre is severely depressed, as occurs with overdoses of opiates or hypnotics, the dose of coramine must exceed that placed on the bottles by the firm. Coramine in these cases not only stimulates respiration but also, by stimulating the cerebrum, decreases the narcosis, which is another expression of the overdose of narcotic taken. As rough rules for guidance, Crohn suggests that a patient who is stuporous, but can be roused, will require about 5 c.c. of the 25 per cent solution intravenously to fully awaken him. The same amount intramuscularly will usually be adequate to restore respiration, and the period of stimulation will come on less abruptly and lasts somewhat longer. If the patient is unconscious and the respiration shallow, either 5 or 10 c.c. intravenously and 5 c.c. intramuscularly, with repetition of the intramuscular injection in half an hour, will usually be adequate. If the patient is still more depressed, the reflexes absent and respiration irregular and failing, still larger doses must be given, either by giving 10-15 c.c. intravenously at once or by repeating smaller doses at very short intervals. As much as 20 c.c. have been given at one time, 20-30 c.c. in two hours. It is obvious that the physician must largely be guided by the patient's response. Doses of 5 c.c. and over, given intravenously, should be given slowly to avoid the production of yawning, cough, vomiting, or even trismus and generalized spasms. In animals, and in extreme cases in man, it is often necessary to approach the convulsive stage which is usually indicated by the first mentioned symptoms. Convulsions, when they occur, are usually of short duration, are not fatal, and can easily be counteracted with ether. Further, it is evident that coramine possesses some depressant actions in doses approaching the convulsant, and hence when using coramine the physician should not attempt to produce and maintain respiration at a normal rate and depth, but merely to make respiration adequate to carry the patient through a dangerous phase of depression.

Cardiazol alone approaches coramine in effectiveness, but its effective and toxic doses lie closer to each other. Coramine is particularly useful if respiratory depression has been produced by any of the barbiturates (barbitone, phenobarbital, pentobarbitone, nembutal, etc.), avertin, chloral hydrate or other hypnotics, alcohol, and opium or its derivatives. It has been used in poisoning by lysol, certain of the toxic mushrooms, carbon monoxide, and uræmia with beneficial results, and in respiratory failure due to ether, spinal anæsthesia or asphyxia neonatorum. Coramine is, then, an emergency drug of the highest possible value, and should be in every physician's emergency kit.

Cardiac and Vascular Effects.—The experimental studies of the circulatory effects of coramine are not entirely in agreement, but the best work indicates that it has little, if any, beneficial

effect on the heart. Blood pressure may rise as a secondary consequence of improved respiration and partly due to the general stimulant effect on the reflex centres, of which the vasomotor centre is one.

It is obvious in reading the early clinical reports on the effect of coramine in cardiac cases, that the authors were not fully aware of the improvement that would be produced in the circulation by an improvement in respiration. Many of the patients with cardiac failure had long been both dyspnœic and cyanosed. In such cases an improvement in respiration would be bound to lead to an improved circulation. In reporting these cases the circulatory improvement was supposed to be purely cardiac and vascular, while in truth a considerable part was probably due to the respiratory improvement. The respiratory centre in such cases is not greatly depressed and will respond to smaller doses than are required in the cases of poisoning referred to above. Yet the literature contains enough cases where circulatory improvement has occurred, to justify a trial of coramine in cases of decompensation with normal cardiac rhythm and dyspnœa. In these cases smaller doses, such as a ½ drachm, t.i.d., per os, seem to prove adequate. Apparently, dramatic effects are not to be expected, but rather a slow progressive improvement, with an increased urine flow as a secondary result.

Some clinical reports have suggested the use of coramine to increase bronchial secretion in emphysema, chronic bronchitis and tuberculosis. Cough does not seem to have been decreased, but becomes looser. There is no evidence which indicates that coramine produces, or would be likely to produce, any such effect by acting on the glands or nerves. It is, however, known to increase the activity of reflex centres, and this might be its mode of action. But other well known drugs might better be used.

Finally, again, attention should be drawn to the stimulant action of coramine on the cerebrum, nasal ganglia, and possibly other parts of the central nervous system, which leads to the awakening of patients from an unconscious or stuporous state produced by the hypnotics and narcotics. It has, in consequence, been used to shorten the period of anæsthesia and depression produced by avertin and other anæsthetic agents. Not only the general physician should have it at hand for emergency use, but also the anæsthetist.

EVIPAN (EVIPAL)

This is the soluble sodium salt of a relatively new barbiturate, with an exceptionally short period of action, probably owing to its rapid destruction by the liver. Hence, if given intravenously in a dose of 7-10 grains it produces a short, 5-25 minutes, anæsthesia. There is in the normal animal, and apparently in man, a wide factor of safety, something between three to four times the necessary anæsthetic dose being fatally toxic. Yet it is not absolutely free from danger, as deaths have been recorded after not excessive doses, though most of these cases have occurred in patients with diseased hearts or a dangerously toxic condition. Further, accompanying its administration certain unfortunate features occur. In many cases there is a very marked relaxation of the muscles of the jaw and tongue, so that the respiratory airway may be obstructed if an assistant does not control the jaw. Secondly, a spasm of the glottis may occur, again obstructing the airway. Thirdly, even during the intravenous administration, muscular twitchings or struggling may occur, which may cause the point of the injecting needle to be pulled out or displaced from the vein, leading to the injection being made into perivenous tissue, with subsequent swelling and pain. Fourthly, the respiratory centre is always more or less depressed, and this, if it occurs in conjunction with a restriction of the airway, may lead to serious asphyxia and an undue cardiac strain. Consequently, no physician should undertake to use Evipan, unless he has available some person who can watch the patient and be ready to assist. Further, the physician should be aware of these dangers and should be fully prepared to meet them. He should have ready for use a laryngeal catheter, and know how to apply it, and have a syringe containing coramine prepared, and if possible carbon dioxide and oxygen. These gases may be readily used from a small mixed tank. The dangers of these mishaps are perhaps greater before the physician has gained experience.

In spite of these dangers, evipan must be a relatively safe anæsthetic for short operations, in view of its wide use and the small number of cases of dangerous symptoms, save in those where the risk was great. This has led an increasing number of practitioners employing it in their cases of minor surgery. It seems to the author to be as safe for the single-handed prac-

titioner, with only intelligent lay assistance, as any general anæsthetic.

The physician must learn how to use it and during the learning process it would be well to have thoroughly good assistance available. Evipan comes in powder, to which sterile water is added to make a solution, usually 10 c.c. in amount. The dose must be adjusted to the requirements of each patient. Various rules have been given. (a) The solution is given slowly, 1 c.c. per minute, while the patient counts aloud till he fails to do so; then as much of the solution again as has been given is injected somewhat more quickly; (b) a variant is to give the first 1½-2 more quickly and then slowly as in (a); (c) to give the solution again slowly till the jaw drops, but Douglas who recommends its use in general practice has usually (100 out of 180 cases) not required enough to cause the jaw to drop. The additional amount given after the failure to count will depend in part on the length of anæsthesia required and the character of the respiration, and must be learned by practice; usually an equal amount suffices. In order to hold the arm still the physician may kneel on the open palm. Naturally the depth of anæsthesia required will also in part depend on the sensitiveness of the region of operation. A small dose of morphine one hour previously makes both the injection easier and the recovery smoother, and leads to the use of a smaller dose. Occasionally, the patient in recovering consciousness is restless and his inhibitions and frequently his judgment are not normal for one and one-half to two hours after awakening.

This drug should be of value to the general practitioner with good judgment for minor surgery. It is easy to see from what has been said about its rapidity of destruction that it would be of no great value as a hypnotic if given per os in the dose recommended.

SODIUM FORMALDEHYDE SULPHOXYLATE

This chemical substance is the result of a prolonged study by Rosenthal in order to find an antidote for mercuric chloride poisoning. It reacts with mercuric chloride, reducing it to the insoluble mercurous form. The experimental evidence and the results of its employment in at least 50 cases of mercuric poisoning seem to indicate that it is by far the best antidote for mercuric salts. Rosenthal is careful to point out that it will presumably do nothing to repair any damage done to the kidney before its administration; all that it can do is to make inert any mercuric salts in the intestinal canal, blood stream, or tissues which has not yet reached the kidneys for excretion, and consequently to prevent further damage. As is evident from the recommended doses, as by direct experiment on animals, sodium formaldehyde sulphoxylate is not a very toxic substance, and any products arising from its decomposition or from its reaction with mercuric salts will be almost harmless. Indeed, most of the sulphoxylate given *per os*, and which does not react with mercuric salts, will not be absorbed but passed. Consequently Rosenthal recommends the following procedure in a case where mercuric salts have been swallowed. As soon as possible wash out the stomach with a 5 per cent solution of the sulphoxylate and leave 200 c.c. in the stomach. That is to say, use at least a quart of water containing 2 oz. sodium formaldehyde sulphoxylate, and of this all but 6 oz. may be withdrawn; the rest should be left to pass down the intestinal canal to neutralize any poison that has passed the pylorus. This is however not enough. Some of the mercury will have been absorbed, and the longer the time that has elapsed, the greater this amount will be. Consequently 10 grams (2½ drachms, more accurately, 154 grains) dissolved in 100 to 200 c.c. (4-8 oz.) should be slowly injected intravenously. "Slowly" means 20 to 30 minutes being taken for the injection. In severe cases another intravenous injection containing 5 grams (75 grains) should be given six hours later. If colitis supervenes, high colon irrigation with 1:1000 solution (1 quart containing 20 grains). If a mercuric poisoning is induced by the introduction of mercury through the vagina, lavage with a weak solution such as is used for colitis should be carried out thoroughly and the intravenous administration should be given. It is important that treatment should be initiated as early as possible. Hence hospitals should have a supply on hand and definite instructions for its use should be prepared. The drug can be obtained from Merck and Co., Winthrop Chemical Co., and the Diarsenol Co.

The number of cases in which it has been used is not as yet large, and consequently an exact valuation of its utility cannot be made. Probably, too, our knowledge of its limitations and the best method of its employment will improve.

DINITROPHENOL

In a study of artificial fever, Heymans, in Belgium, showed that any organic nitro-derivatives produced fever. Tainter, in California, undertook the study of the simplest of these substances, alpha-dinitrophenol. He showed that dinitrophenol increased metabolism; if a large dose is given, fever occurs, but that even in doses smaller than those causing fever metabolism was increased, the basal metabolism rising 10-50 per cent. As a result of the increased oxidation animals and man lose weight. The respiratory volume is somewhat increased, in most cases to an extent not noticed by the individual, without an increase in cardiac rate or in rectal or mouth temperature. The increase in metabolism apparently occurs largely in the liver and abdominal organs, but to some extent in the muscles. It appears that fat and carbohydrate are largely burned, and the consumption of protein is but little increased, as is the case if thyroid is given. In small doses, 3 mg. per kilogram, reduction in weight occurred slowly, at the rate of 2 to 3 lbs. per week. Most of the patients in a series (113) showed no symptoms, yet a certain proportion did so. Some (20 per cent) complained of warmth or shortness of breath; some 6 felt tired and 4 dizzy; 8 suffered sooner or later from skin disturbances. (In a larger series these formed some 25 per cent). The prodromal symptom was intense itching, which was followed by urticaria or a maculopapular rash. Some of these patients, after an interruption of treatment, were able to take the drug again without recurrence of skin disturbance. The most common type of undesired reactions to chemicals of the general group of which dinitrophenol is a member is a skin disturbance, and it is not astonishing that these reactions should occur, but rather that having once occurred in any patient they do not recur.

There is no doubt that dinitrophenol has been taken by a great many persons. Very many must have taken dinitrophenol under medical control, and many more independently of medical advice, as it has been freely sold in drug stores in the United States under its own name and in proprietaries (Slendite, Dinitropenol). Tainter estimates the number at 100,000. It is therefore remarkable that so relatively few cases of serious poisoning have been reported. Cases of toxic jaundice and agranulocytic leucopenia, have been described, even in cases when apparently safe doses have been used, and recently some six or seven cases of rapidly developing cataract. The use of the drug undoubtedly entails a risk, and there is no doubt that, firstly, the drug should only be obtainable on a physician's prescription, and, secondly, that the physician should be prepared to study his patient carefully and thoroughly during treatment.

Further questions must be considered. First, is the exhibition of such a drug worth while, when in most cases dietary measures will produce the same result more safely if the cooperation of the patient is maintained? particularly, if one considers that many patients, when they have got used to the new diet, find that they are so much better that they are prepared to persist, and also when one considers that long continuance of the drug greatly increases the risk, and consequently that treatment with it must be temporary. A loss of 2 lbs. a week can be achieved by a not very great restriction in the diet. These considerations have led many clinics to abandon the use of this drug entirely. The second question has not been as yet settled, namely, does dinitrophenol lead to an increase in the normal metabolism or does it lead to an abnormal one? Some evidence is accumulating that the latter is the case, and if this be demonstrated clearly there is a further reason why it should not be used.

It seems obvious that the use of dinitrophenol to reduce obesity is not justified, save perhaps in very exceptional cases, and then only if the patient can be kept under close and detailed scrutiny by a trained physician.

ACUTE POST-OPERATIVE PAROTITIS.—J. M. Robinson and J. Spencer report the results of x-ray therapy in twelve cases of acute parotitis following laparotomy. All cases were treated with deep x-rays—namely, 200 kV, filtered through 0.5 mm. of copper and 1 mm. of aluminium and administered to one or both parotid glands through a cone of 10 cm. diameter. The optimum dose was found to be about 300 *r* units delivered to the lesion in one sitting. The results indicate that this form of therapy will definitely reduce the high mortality associated with this infection. The most striking results were observed in those cases which were treated soon after the first evidence of inflammation of the gland. As a rule the pain was rapidly relieved and suppuration was prevented. For several reasons the authors prefer x-rays to radium in the treatment of this affection.—*New Eng. J. Med.*, 1936, p. 150. Abs. in *Brit. M. J.*

VOLVULUS OF THE SMALL INTESTINE

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MY object in presenting this paper is, firstly, to report a case of volvulus of the entire small intestine, and, secondly, to summarize the literature on this relatively rare form of intestinal obstruction. Numerous isolated reports have appeared in the past thirty years on the condition, but little attempt has been made to consider it in its entirety.

ETIOLOGY

Normal small intestine cannot undergo a pathological extent of torsion, and some predisposing cause always exists, the volvulus being secondary. Numerous theories have been propounded to account for the condition, and these can be conveniently divided into congenital and acquired. Each is correct in explaining a certain group of the cases and will consequently be taken up separately. First let us discuss the physiological aspect.

In the Bradshaw Lecture of 1928, Fagge[1] deals with the question of torsion chiefly as it pertains to pedunculated intra-abdominal organs, but his remarks also bear on the subject in hand. He quotes the theory of Fischer that rotation is a natural form of growth, the tissues developing under constant spiral axial torsion, the best example of which is the fetal umbilical cord. However, Fagge places little belief in this as the causative agent in volvulus, and states that rotation is rather a process where two distinct factors are necessary (a couple). For instance, in pelvic tumours, he believes that the couple is intestinal peristalsis and a contracting uterus, or, in upper abdominal torsions, intestinal peristalsis and the anterior abdominal wall.

The principles concerned, according to Meyer, are the transmission to the organ or tumour of a turning movement of the whole body, the torsion resulting from the property of inertia of the tumour by which it remains in the new position when the body has returned to rest. At this point I may say that the degree of rotation is not entirely constant with the degree of vascular obstruction. Severe nutritional disturbances have been reported in tumours twisted at 120° and no symptoms in others with a torsion of one complete turn.

Congenital causes.—These are responsible for all the cases I have been able to collect of volvulus of the entire small bowel. The case about to be reported also falls into this category.

First let me mention a few major facts in the embryology of the intestine. The intestine is divisible into three parts, the foregut, which forms the pharynx, œsophagus, stomach and duodenum as far as the opening of the bile and pancreatic ducts; the midgut, which is formed as a U-shaped loop provided with a mesentery, the latter attached by a narrow base to the posterior abdominal wall. This portion forms the third and fourth parts of the duodenum, jejunum, ileum, cæcum, ascending and right two-thirds of the transverse colon. This whole area is supplied by the superior mesenteric artery. The hindgut forms the remainder of the large intestine, including the rectum. In the rotation of the gut the part developed from the post-arterial limb of the mid gut (comprising the last three feet of the ileum, cæcum, ascending colon and right two-thirds of the transverse colon), which is originally on the left side of the abdomen, swings over in an anti-clockwise direction with the superior mesenteric artery as an axis, the cæcum being carried from the left upper quadrant of the abdomen to the right near the gall bladder, where it remains till about the time of birth, the cæcum then migrating to the right iliac fossa. The mesentery of the U-shaped loop is at first only attached to the posterior abdominal wall where the superior mesenteric artery enters it, but during the fourth and fifth months of fetal life a secondary more extensive fusion (zygosis) occurs to the posterior wall. The last part of the mesentery to become adherent is that near the ileo-colic junction and this portion may remain free altogether and thus produce the condition of floating cæcum.

This now explains the most common congenital cause, when it is found that in cases of entire small bowel volvulus the attachment of the mesentery to the posterior abdominal wall has been lacking completely, except at the spot where the superior mesenteric artery enters. This results in an abnormally mobile bowel subject to all the physiological influences before mentioned. Gordon Taylor[2] believes that in almost every case of complete volvulus the twist has been a continuation of the normal movement of rotation, the cæcum being twisted behind the small bowel mesentery, presenting finally in the left upper quadrant. However, this has not been borne out by subsequently reported cases where the volvulus has been more frequently in a clockwise direction rather than anti-clockwise.

Another possible cause which has been mentioned by previous writers is an abnormally long mesentery. In all cases where such a condition has been reported, the extent of volvulus in the bowel was only a segment and could only be so, as the mesentery, though elongated, had its normal posterior peritoneal attachment. Thus we have a logical congenital cause for both the partial and complete types.

Acquired conditions.—In this category I could find no account of a complete small bowel volvulus; all were partial. This partial type is more common than the complete, and justly so, considering the great variety of predisposing causes. The principle of this form of volvulus is that the bowel becomes fixed at one point only and the remainder of the loop rotates about that spot as the axis. The most common predisposing causes of this type are, a knuckle of bowel caught in a hernial sac, post-operative adhesions, and adhesions of the bowel to a pelvic viscus, as in the case reported by Hamilton Bailey, where the bowel was adherent at one spot to the fundus of the uterus and rotation had covered about that axis.

In the three cases presented by Gordon Taylor,[2] one was a volvulus of six feet of small intestine due to a hernia, one was a post-operative case due to adhesions, and a third a complete volvulus of small intestine and cæcum due to a congenital lack of fusion of the mesentery to the posterior abdominal wall.

Incidence.—Vaughan,[3] in 1903, collected 61 cases of volvulus of the intestine, and stated that 30 per cent affected the small intestine, the sigmoid ranking first and the cæcum second in order of frequency. He found that in 21 of his series the whole of the small intestine was affected. The St. Bartholomew's Hospital records up to 1915, reported by Isaacs,[4] showed 25 cases stated to be due most commonly to a congenital defect. However, whether partial or complete was not divulged. The odd point about these cases is the fact that, though caused by congenital defect, there were only 2 patients under twenty years of age; 12 were between 20 and 50 years; 10 between 50 and 70 years; and 1 over the latter age. Sixteen patients were males and 9 females. In Weible's[5] series of 64 cases, 51 were males and 13 females. However, there are 2 cases reported in the literature, by Fletcher[6] and by Trillat and Boulez,[7] of volvulus of the complete small intestine in new-born children. Mudenee, of the Massachusetts General Hospital, in a report over a period of twenty years of 239 patients with intestinal obstruction found 29 with volvulus, 10 being in the small intestine (4 per cent). In the London Hospital during 13 years there were 669 cases of intestinal obstruction, of which 27 were volvulus involving the small intestine (4 per cent).

SYMPTOMATOLOGY AND TREATMENT

These patients are almost invariably sufferers from severe constipation, the one reported here having only two bowel movements a week. The onset does not appear to have any definite relation to strain or movement, frequently occurring when the patient is at rest. Constipation for a longer period than usual commonly precedes the onset. Definite spasmodic attacks of colicky pain occur generalized throughout the abdomen. Vomiting soon occurs, and the remainder of the symptoms, which are indistinguishable from those of small bowel obstruction from any cause, develop in proportion to the severity of the volvulus. The diagnosis is almost invariably small bowel obstruction of unknown cause, and laparotomy is performed. Gangrene and the necessity for resection is found usually in those cases of partial volvulus of the acquired type, and the prognosis varies with the severity of the twist and the general condition of the patient. The congenital types seldom progress to the extent of causing gangrene, or else are slower in their progression so that they do not reach the stage of gangrene before operation is performed.

In 1924, Wheeler[8] found that among 77 reported cases were 25 recoveries, all following operation. Stacy,[9] in 1932, reported three cases of volvulus of the small intestine, two of which were in a clockwise direction, all cured by operation.

There is little difficulty in recognizing the cause of the localized form, but the operator may find himself puzzled when, in the complete type, he sees nothing but a mass of distended bluish small gut. The condition is ascertained on finding the free edge to the mesenteric root pushed forward towards the anterior abdominal wall and that no mesenteric attachment is encountered. The superior mesenteric artery can be seen and felt in the free edge of this abnormal mesentery. In such findings a twist of the mesentery can be made out, usually about 180°, and most com-

monly clockwise. The condition cannot be corrected by individual reposition of various loops, but by mass rotation of the small intestine back to the normal position. To effect this, evisceration is necessary. Fixation after reposition is not advisable, as the condition rarely recurs, and also the operation is prolonged by attempts to suture the free edge to the posterior abdominal wall, a difficult and dangerous procedure, the superior mesenteric artery being in danger of wounding due to the field obscured by distended coils. I have been unable to find any case where recurrence has occurred in the congenital type after operative correction.

CASE REPORT

J.McT., referred by Dr. MacIntosh, was admitted to the Huddersfield Royal Infirmary on April 14, 1936, giving a history of life-long constipation, with a bowel movement about twice a week. No previous attacks of abdominal pain; no previous operations; no relevant past illnesses.

At 3 a.m. on April 13th he was awakened from sleep by colicky abdominal pain centred around his umbilicus. This continued as spasmodic crampy pain and soon caused vomiting. Pain and vomiting continued intermittently all that day and the day of admission. No bowel movement for three days. No urinary symptoms.

Physical examination.—Temperature, 98°; pulse 96; respiration, 20. The heart was enlarged to right and left; marked aortic insufficiency, with Corrigan pulse. Blood pressure, 155/40. (The blood Wassermann test later proved negative.)

The abdomen presented the usual signs of small bowel obstruction. The diagnosis was acute small bowel obstruction of doubtful origin.

Operation.—Under spinal percaine. Right paramedian incision. On opening the peritoneum distended bluish small bowel was seen, with considerable amber-coloured free fluid. The bowel showed numerous small petechial hæmorrhages. The cæcum was in normal position and collapsed, as was about six inches of ileum, which could be seen disappearing beneath a mesenteric shelf. Apart from this small portion, the entire small bowel was found to be involved. Examination of the first part of the jejunum revealed a similar picture, with the first three inches disappearing beneath the free mesenteric edge. A hand passed across the posterior peritoneal wall could find no posterior mesenteric attachment, the only point of contact being at the spot where the superior mesenteric artery entered. This free sickle-shaped edge of the mesentery was pushed forward towards the anterior abdominal wall and the artery could be felt pulsating at the free margin. A mesenteric torsion was recognized and found to be about 180° in extent. The patient was eviscerated and the clockwise twist reduced by opposite rotation. Bowel colour improved and gas flowed into the small portion of contracted ileum. Recovery was uneventful.

SUMMARY

Small bowel volvulus is considered, giving:—

1. Some physiological theories on torsion in general, and bowel in particular.

2. The etiology is divided into congenital and acquired cases, with embryological explanations of the congenital type.

3. The incidence is discussed, revealing volvulus of the small bowel to be the least common type encountered and to be more common in males than females.

4. The operative recognition of the condition and the treatment are described.

5. A case of volvulus of the entire small intestine of the congenital type is presented, with the operative findings.

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PRESENT STATUS OF FEVER THERAPY PRODUCED BY PHYSICAL MEANS.—F. H. Krusen states that during the past year the use of fever produced by physical means has been recommended for no less than fifty different diseases. The results in the treatment of the majority of these diseases have not been encouraging, although for a selected few the method of treatment has given promise of great usefulness. The studies which have been made during the last year indicate that its chief sphere of usefulness lies in the treatment of gonorrhœa, both acute and chronic, and its complications. It would appear that it may be of value in the treatment of syphilis in its various manifestations, particularly when it is combined with chemotherapy. While there is a suggestion that artificial fever produced by physical means may be helpful in the treatment of intractable bronchial asthma in selected cases of chronic infectious arthritis, chorea and undulant fever, nevertheless clinical data are not sufficient to permit any final conclusions. Its value in about forty other diseases remains to be proved. Hæmorrhagic encephalitis has occurred in some instances, and hæmorrhagic pneumonia also has been noted. Deterioration and hæmorrhage may occur in the cortex of the adrenal glands. Death may occur as the result of vascular collapse. In subacute bacterial endocarditis there is apparently danger that fever therapy may produce multiple emboli. The production of fever by physical means is strictly a hospital procedure; and it is essential that a well trained personnel be in complete charge of the work. Patients to be treated with fever should be selected with as much care as are patients who are to undergo a major surgical operation. It would seem quite apparent that, for the present, the medical profession as a whole should avoid the use of fever therapy unless there is available an institution properly equipped to administer this type of treatment.—*J. Am. M. Ass.*, Oct. 10, 1936.

ROENTGEN RADIATION TREATMENT OF CHRONIC COUGH OCCURRING DURING CHILDHOOD

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BOWDITCH, Leonard and Smith[1] in 1924 reported upon the use of roentgen radiation in the treatment of coughs occurring in children during the active stages of pertussis. The results which they obtained were not only satisfactory but clearly indicated that no untoward effects were to be expected. Their experience prompted us to treat all children with chronic cough in whom all possible etiological factors save pertussis had been excluded, children who had failed to respond to the other available forms of treatment. The authors referred to were of the opinion that they had been able to obtain their results by producing a reduction in the size of the tracheo-bronchial lymph nodes. We reasoned, therefore, that satisfactory results should be possible in the treatment of children with chronic cough of unknown etiology, if it were assumed that the cough under such circumstances was due to enlargement of these nodes.

When the use of roentgen radiation in the treatment of pertussis was first recognized there were, naturally, many who considered that this form of treatment, even if effective, carried with it some element of danger. The ill effects which were looked for were chiefly two: constitutional, and possible effect upon the thyroid gland with its consequences. No such changes were noted when the doses of radiation recommended by Bowditch, Leonard and Smith were employed. It is worthy of note that Minot and Spurber were unable to demonstrate any blood changes following that amount of radiation. Friedman and Blumgart, too, who have radiated normal thyroid glands, were unable to alter their patients' metabolic rates or the architectural structure of the glands. On some occasions they had given as much as 4,000 r units in nineteen days. In two instances nine-tenths of the normal gland had previously been removed in an attempt to lower the metabolic rate. These experiences, and others which are not recorded here, confirmed Bowditch, Leonard and Smith's contention that no ill effects followed radiation treatment.

The studies recorded here were started in 1924. Sufficient time has, therefore, elapsed to permit of trustworthy conclusions. Over 700 children have been treated to date. It becomes obvious then that the types of chronic cough of childhood under consideration constitute a very definite problem; for the majority of the children were referred to us after all other known therapeutic measures had been tried without success. It should be equally obvious that the early results justified the continued use of this form of treatment.

Complete physical and radiographic examinations were carried out upon the first 100 children who were treated. All known causes for cough were searched for, and any child presenting a cough of known etiology, other than that it followed pertussis, was excluded. Our first series of cases were chiefly those occurring in children who gave a definite history of whooping-cough followed by a persistent cough which lasted anywhere from eight weeks to many months after the acute stages of the disease had subsided. In many instances, the symptoms suggested a recurrence of the disease.

Positive roentgen-ray findings were not the rule in the children we treated. Increased width of the hilus shadow was observed on some occasions, but in most instances there were no demonstrable changes. It was, therefore, impossible to prove that any favourable response to treatment was due to any demonstrable changes in the lungs or hilus regions. Our problem then became one of treating a symptom. However, it was appreciated that the beneficial effect might be dependent upon a variety of factors. The numerous theories which had been advanced in explanation of the beneficial effects obtained by roentgen radiation treatment of pertussis bear witness to this fact. These theories will be discussed later, and only

those which bear some reference to the problem will be considered. In order to compare the effects of one form of radiation with another 10 children were treated with ultra-violet radiation. The results obtained by roentgen radiation were so much better that ultra-violet treatment was abandoned.

The technique follows very closely that used by others in the treatment of whooping-cough: 111 K.V. 4 Ma. 50 cms. S.T.D. 4 mms. aluminum filter. The treatments were given to the back and front of the chest alternately, the total being four treatments, two behind and two in front. The total number of r units given ranged from 135 to 225 r units, slightly more than one-fifth to slightly over one-fourth of an erythema dose to each skin surface. The size of the aperture was altered slightly, depending upon the size of the child's chest, varying from 7 to 9 cms. in diameter. The central ray was directed over the hilus regions, both back and front. All four treatments were given on consecutive days with satisfactory results. However, under most circumstances it is advisable to use the longer period of time in distributing the treatment.

It is evident that accurate statistics of the percentages of cures are quite impossible because of the many factors which might tend to affect the results both favourably and adversely. For example, on those occasions when the results were extremely favourable, it can be suggested, and rightly so, that the children might have stopped coughing spontaneously at some time during the period of treatment. By the same token, however, any intervening acute upper respiratory tract infection could have prolonged the coughing in spite of the radiation.

In the first series of 100 cases already referred to the results were gratifying. There were no untoward reactions. It is safe to state that 80 per cent of the children so treated were definitely relieved of their coughs or obviously benefited. Less than half of the remaining 20 per cent failed to respond to the treatments. In a subsequent separate series of 77 cases, where it was possible to follow the end-results even more closely, these were eminently satisfactory and confirmed the impression that this treatment is of value. Following either the first or second treatment in about 50 per cent of the cases there was a definite exacerbation of the cough. This reaction, however, was of short duration, rarely exceeding forty-eight hours. In this latter group, based on the experience with the first group of cases, one could prognosticate a favourable response almost without exception. This favourable response occurred usually from four to five days after the final treatment.

The two case reports which follow are striking illustrations of the possible response to radiation. The first is particularly instructive because of the unusually long clinical history of illness and because the results obtained with radiation were so rapid, yet so permanent. In this instance, there is little doubt that the beneficial results were directly attributable to this form of therapy.

CASE 1

J.T., male, aged 8 years, whose family and personal past history were both irrelevant, at the age of 3 years developed whooping-cough. This illness was of unusually long duration, and his cough continued severe and spasmodic long beyond the usual course of the disease. Throughout his entire illness of five years' duration his chronic cough simulated that which is characteristic of whooping-cough. With the onset of warm weather his cough subsided, but only temporarily. Physical and radiographic examinations of the chest were entirely normal six months after the onset of his attack of pertussis, as were numerous protein sensitization tests. During the winter months of the years 1925 to 1928 inclusive, this child was taken to a warmer climate, and while there obtained some relief. When he came under my care in 1929 his cough was again present and was just as severe as it had been in the past. Physical and radiographic examinations were again essentially negative. There was questionable peri-bronchitis, but the tracheo-bronchial lymph nodes were not noticeably enlarged. Roentgen radiation was suggested and the treatments given. On the evening following the first treatment the cough was decidedly more severe. The second treatment was given two days later. That evening the child was free from cough. Two more treatments followed and no further changes were noticed. His cough had entirely disappeared.

This boy has been observed at intervals since the winter of 1929 and there has been no recurrence of his chronic cough for which he was treated. He has had the average number of upper respiratory tract infections, but they have run the expected course. No ill effects as the result of the treatments have been manifested.

CASE 2

A female, aged 10 years. Family and past history unimportant. Whooping-cough sixteen weeks previously to the commencement of roentgen radiation treatment. Since the onset, the paroxysms of coughing have persisted throughout, being at all times as severe as they were during the active stages of pertussis. The severe paroxysms were accompanied by vomiting and as a consequence emaciation was marked. During the ten days previous to the beginning of roentgen radiation, the cough seemed to have become even more severe. The child also had four convulsions during this period. Save for the emaciation, the general physical and radiographic examinations of the chest were normal. Four treatments were given in as many days to the back and front of the chest alternately. As in every case the treatment

was given over the hilus regions. Both cough and convulsions ceased four days after the last treatment and up to the present time have not returned. This child is now in good health, more than four months after the last treatment.

These two cases are included in the series of 77 cases referred to previously. The greater number of the patients in this series showed a similarly favourable response to treatment, but in a somewhat less dramatic manner than in the two cases cited.

The total number of patients treated to date is over 700. Mention has already been made of the results obtained in the first group of 100 cases and in the selected group of 77 cases. The results obtained in the larger remaining group are practically identical. Many of these cases, approximately 40 per cent of this largest group, concern children whose cough followed acute upper respiratory tract infections, which were in no way attributable to pertussis. As in the first group, save when the cough was definitely known to be an aftermath of pertussis, all other etiological factors were excluded before roentgen radiation was used.

As indicated earlier in this discussion, this work was based on the hypothesis that beneficial effects in alleviating or eliminating chronic coughs in children might be obtained by reducing the size of the tracheo-bronchial lymph nodes. Yet, from the beginning no gross enlargement was observed in those cases selected for treatment. It was felt at that time that possibly there might be sufficient enlargement of these glands to cause cough and yet insufficient to be evident on radiographic examination. Appreciating this fact, it was decided to go on with this work although we were uncertain as to whether or not response to treatment could be judged in any other manner except by symptomatic response. The rapid response to treatment tended to confirm our suspicion that our original hypothesis, namely, shrinkage of the tracheo-bronchial lymph nodes, was incorrect.

Ivy, Orndoff, Jacoby and Whitely[2] experimentally showed that no changes in the lymph glands could be demonstrated histologically before fifteen days after the glands had been irradiated. They also noted that it took about sixty days for fibrosis to take place. von Mysenburg[3] thought that in pertussis the radiation effects were due to its action upon the bronchial ganglia and bronchial mucous membranes. Picherle thought that the effect was directly upon the bronchial mucous membranes, thus diminishing the presumed increased irritability of the nervous system. Some believed that the auto-protein inoculation by the products of radiation was the means of producing the favourable reaction in alleviating the cough. Smith thought that there was an indirect effect caused by the influence of the radiation upon the thyroid and thymus glands. Gouin and Bienvenue[4] were of the opinion that the radiation had a sedative effect upon the vagus. Others believed that the reaction to radiation was directly due to the effect upon the vegetative nervous system. This belief is further enhanced by Langer's[5] early animal experimentation with radiation of the vegetative nervous system. Later he claims to have substantiated the experiments by his clinical results in a rather varied group of diseases.

It is obvious from the multiplicity of theories that convincing proof of the action of roentgen radiation, particularly in relation to relieving coughs in children, has yet to be established. In our work, we could not definitely confirm any of the theories advanced. Langer noted that following radiation of the vegetative nervous system in certain definite segments there was an accentuation of the symptoms for which the patient presented himself. He called this reaction "stage 1, or the stage of irritation". This was followed in a few days by distinct improvement and in many instances complete relief from all symptoms. This, in a measure, corresponds to many of the reactions noted in the children treated for persistent cough. In addition, the radiation was directed over the hilus regions, which would very well include the peribronchial ganglia.

No local or general harmful effects have resulted from this form of treatment carried on over a period of ten years. During that time we had the opportunity of treating over 700 children. This indicates not only that there was the need for a form of treatment other than those available, but also that it proved to be the best method for the type of cases described, at the present time. It is not to be assumed from the above that roentgen radiation is advocated for all forms of cough in children. Emphasis must again be laid upon the fact that

all etiological factors be as carefully eliminated as possible.

SUMMARY

Seven hundred children with persistent cough were treated with roentgen radiation. This form of treatment was found to be of distinct value when the cough was either an aftermath of pertussis or subsequent to an acute upper respiratory tract infection.

The amount of radiation used was small. No injurious effects were noted.

No child with a chronic or persistent cough should be treated by roentgen radiation before all etiological factors have been satisfactorily eliminated.

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THE TREATMENT OF INFANTILE SCURVY WITH ASCORBIC ACID

(PRELIMINARY REPORT)

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IN 1932 a Hungarian scholar, Albert Szent-Györgyi discovered the chemical constitution of vitamin C. After numerous experiments he showed that this vitamin is constituted essentially of ascorbic acid. Afterwards chemists at Birmingham studied its constitution, and Reichstein succeeded in synthesizing it, and it is now possible to administer ascorbic acid orally in tablet form.

Even if it be true that infantile scurvy is now a rare condition, the physician nevertheless has occasion to practise prophylactic medicine in scurvy by prescribing for infants, as young as 3 months, small quantities of fruit juice. In these conditions it is not rare to find young children who refuse to take orange or tomato juice, or who, apparently, tolerate it poorly. It is in these conditions that tablets of ascorbic acid can be of service to the practitioner. We believe it of benefit, therefore, to bring the new mode of administration of vitamin C to the attention of our confrères.

In order to ascertain for ourselves the therapeutic value of ascorbic acid tablets we have employed them exclusively in the treatment of 6 cases of infantile scurvy which we have recently observed in our service at the Misericordia Hospital.

CASE 1

B.G., female, aged 7 months, weight 12 pounds, was seen on March 6, 1936, having pains in the lower limbs; swelling of the eyelids, with ecchymosis of the left lid; slight anæmia: hæmoglobin, 50 per cent; red blood cells, 3,400,000. Treatment was with ascorbic acid (Cebione), one-half of one 5 centigram tablet twice a day. No change was made in the diet. She was cured after thirteen days of treatment (March 6th to 19th), all the signs having disappeared. The anæmia seemed to be little affected by the treatment. Actually a second count made March 19th showed little change: hæmoglobin, 50 per cent; red blood cells, 3,650,000.

CASE 2

G.C., male, aged 11 months, weight 15 pounds; suffering from pains in the lower limbs, March 14, 1936. A slight hæmorrhagic gingivitis, coincident with teething, was found on clinical examination, also an anæmia of medium severity: hæmoglobin, 48 per cent; red blood cells, 2,700,000. Treatment was with ascorbic acid (Cebione), one-half of one 5 centigram tablet twice a day. No change in diet. Cure after fifteen days of treatment (from March 14th to 29th). The pain in the limbs and the hæmorrhagic gingivitis disappeared, and there was considerable improvement in the anæmia: hæmoglobin, 55 per cent; red blood cells, 4,200,000.

CASE 3

S.E., female, aged 9 months; weight 15 pounds; with pains in the lower limbs March 16, 1936. Upon examination of the infant slight anæmia was noted: hæmoglobin, 55 per cent; red blood cells, 3,825,000. Teething was little advanced. Only one lower left middle incisor; there was no hæmorrhagic gingivitis. Treatment was with ascorbic acid (Cebione) one tablet, 5 centigrams, twice a day. No change in diet. Cure occurred after thirteen days of treatment (from March 18 to 31, 1936), with disappearance of the pain in the lower limbs. Anæmia, however, is little changed by the treatment: hæmoglobin, 50 per cent; red blood cells, 3,650,000.

CASE 4

R.D., male, aged 12 months. On March 19, 1936, he had pains in the lower limbs, slight hæmorrhagic gingivitis, and a moderate anæmia: hæmoglobin, 45 per cent; red blood cells, 3,500,000. Treatment was with ascorbic acid (Cebione), 5 centigrams, twice a day. No change was made in diet. He was cured after eighteen days (March 19 to April 6, 1936), as indicated by disappearance of the pain in the lower limbs and of the hæmorrhagic gingivitis. With regard to the anæmia there was no change: hæmoglobin, 45 per cent; red blood cells, 3,500,000.

We noted in this case that the hæmorrhagic gingivitis disappeared after ten days of treatment, the pains in the lower limbs eight days later.

CASE 5

H.E., male, aged 9 months, weight 16 pounds, suffered from pains in the lower limbs, February 20, 1936. At this time a typical hæmorrhagic gingivitis and purpura were found. Slight anæmia: hæmoglobin, 45 per cent; red blood cells, 3,500,000. Treatment was with ascorbic acid (Cebione), one-half tablet of 5 centigrams, twice a day. No change was made in diet. Cure occurred after eleven days of treatment (from February 20 to March 2, 1936), with disappearance of pain, the hæmorrhagic gingivitis, and the purpura. Anæmia was improved by the treatment: hæmoglobin, 50 per cent; red blood cells, 4,575,000.

It was noted in this case that the hæmorrhagic gingivitis preceded by several days the pains in the lower limbs and that it coincided with the cutting of a tooth. Furthermore, this child refused to take tomato juice.

CASE 6

F.D., male, aged 10 months; weight 15 pounds; on February 20, 1936, had pains in lower limbs. Clinical examination revealed a slight anæmia: hæmoglobin, 48 per cent; red blood cells, 3,550,000. No hæmorrhagic gingivitis (the child had no teeth). Treatment was with ascorbic acid (Cebione) in dosage of one-half of a 5 centigram tablet twice a day. No change was made in diet. Cure occurred after eleven days of treatment (from February 20 to March 2, 1936), as evidenced by disappearance of the pain in the lower limbs. The anæmia was little influenced by the treatment: hæmoglobin, 50 per cent; red blood cells, 3,750,000.

As we have seen, the action of ascorbic acid in infantile scurvy is remarkable. Most of our patients, we cannot say all, were cured by this treatment alone in less than fifteen days. The only exception to the rule was No. 4. In this case cure was effected after 18 days of treatment. It is hardly necessary to add that the hæmorrhagic gingivitis disappeared on the 10th day. Only the pain in the lower limbs, and we know the difficulty of its determination in young children retarded the definite cure, and we were obliged to continue the treatment to the 18th day.

From these six observations one can conclude the real value of ascorbic acid tablets in the treatment of infantile scurvy. One should use the tablets not only in treatment of scurvy of young children, but also as a prophylactic measure when they refuse or tolerate fruit juice poorly.

The "Cebione" tablets were kindly supplied by Merck and Company Limited, Montreal.

XANTHOMATOSIS AND SUDDEN DEATH.—F. Harbitz gives an account of several cases of xanthomatosis common to all of which was the sudden death of the patients. In one of his police cases he was called on to investigate the cause of death in a man, aged 46, with a previous record of apparently perfect health. He had left home on skis alone, and had been found dead, face downwards, with his skis still on and a broken ski stick under him. There were slight and insignificant scratches on his face, but no lesion of the skull or brain could be found post mortem. A clue to the cause of death was found in almost symmetrical swellings on the backs of both hands. These swellings were yellow, nodular, and rather hard, presenting the characteristic features of xanthomata. Similar swellings connected with the periosteum were demonstrable over the olecranon on each side. A search was made for other manifestations of xanthomatosis, and when the hypertrophic, fat-infiltrated heart was opened, yellowish-white deposits were found in both coronary arteries, the lumen of which was reduced in several places. Similar deposits, of a bright yellow colour, were also found in the aorta, just above the aortic valve, and also in the abdominal aorta. Some of these yellow deposits had broken down and ulcerated. It is possible that a fall, entailing a blow on the head, may have precipitated the fatal issue, but its prime cause must be regarded as the xanthomatosis. In two other of the author's cases, multiple xanthomas under the skin were observed in childhood, and both patients died suddenly at the age of 22. After referring to yet another case, published by a compatriot in 1932, Professor Harbitz suggests that the connection between xanthomatosis and sudden death is frequent enough to warrant its general recognition. — *Norsk Mag. f. Laegevid.*, July, 1936, p. 695. Abs. in *Brit. M. J.*

STREPTOCOCCUS MENINGITIS

(WITH A REPORT OF EIGHT CASES: TWO RECOVERIES)

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STREPTOCOCCIC meningitis offers a difficult problem. While the diagnosis affords no particularly serious difficulties, once the disease is firmly established, the results obtained by various methods of treatment have been extremely discouraging. The mortality rate apparently is over 97 per cent. Fortunately the disease is rare. Gray[1] in a comprehensive review of the literature on the subject lists only 66 cases in which recovery was reported. In 44 of these cases the diagnosis was confirmed by the finding of the streptococcus in the spinal fluid.

The majority of cases of streptococcic meningitis arise from some focus of infection in the head, most frequently from a purulent otitis media. Infection in the nasal accessory sinuses accounts for a considerable number of cases. Meningitis is also one of the dreaded complications that may occur following trauma of the skull, especially a fracture involving the frontal sinus, an injury not infrequently associated with motor accidents. Six of the reported recoveries occurred in scarlet fever patients in whom streptococcus meningitis had occurred as a complication of scarlet fever. Some maintain that a streptococcus meningitis may be of hæmatogenous origin, and that the streptococcus may settle in the meninges without any focus of infection being detected; I have not seen such a case. On occasion localization in the meninges may occur in the later stages of a streptococcus septicæmia and in my experience this is the most serious complication of septicæmia. Also, a coincident invasion of the blood stream and of the meninges with streptococci may occur, particularly when the infection is overwhelming and arises from some focus close to the brain.

An invading streptococcus may give rise to a localized meningitis, a diffuse meningitis, or a brain abscess. The nature of the inflammatory defensive reaction that occurs in and about the meninges apparently has but a limited influence on the final outcome. Nor has sufficient evidence been disclosed that the virulence of the strains of the causative streptococcus affects to any particular degree the high mortality rate. Apparently, numerous strains of streptococci capable of producing inflammation in the surrounding tissues and capable of extended invasion are virulent for the meninges. It is possible, of course, to select a streptococcus which exhibits a high degree of virulence when introduced experimentally into the meninges of lower animals, and in the rapid and overwhelming invasions which one so frequently sees in meningitis it is conceivable that the virulence of the organism plays a more important part than the lack of resistance in the host.

The virulence of the organism and the defensive mechanism of the host are of much greater import in the prevention of the extension from the original focus. The excessive mortality indicates that once the invasion has reached the meninges further resistance of the host is practically negligible. Clearly, the particular value of host resistance lies in the ability to prevent or to confine within narrow limits the invasion of the microorganism. These concepts should be an aid in determining the methods of prevention and treatment of the disease.

Obviously the most important matter is prevention. The accepted surgical and medical procedures for dealing with foci of infection are indicated. However today it is recognized in relation to surgical procedures for the treatment of streptococcic infections, such as the draining or extirpation of a focus, that while adequate drainage or extirpation may be considered necessary, yet injury to adjacent normal tissues increases the risk of extension of the infection. Moreover, even with the most exacting care and technique in dealing with foci of infection in the head extension to the meninges may occur; also, invasion of the brain with a streptococcus occasionally complicates a relatively simple procedure such as a submucous resection or a tonsillectomy.

The question of the prophylactic use of serums or vaccines arises. Kolmer[2] suggests the prophylactic use of vaccine in chronic ethmoiditis and sphenoiditis as well as in chronic otitis media, preferably autogenous vaccines, to be administered over a period of six to eight weeks, in order to raise immunological resistance preliminary to operation. I have carried out this procedure with eleven patients and no complication followed operation. Kolmer and Amamo[6] also demonstrated that in an experimentally produced meningitis of the lower animals the prophylactic use of specific antiserums was of value. The difficulty arises from the inability to obtain a specific antistreptococcic serum. This difficulty I have attempted to overcome by developing a colony of rabbits highly immunized to various strains of streptococci. In trauma of the skull, especially if associated with fracture involving the frontal sinus, a prophylactic inoculation of antistreptococcic and antistaphylococcic serum is indicated in order to supply a temporary passive immunity.

No standard methods for the treatment of meningitis exist. A review of those employed in the fortunate cases of recovery indicates a wide range and diversity of therapeutic agents and measures. These include simple lumbar tap, frequent taps, cisternal drainage, continuous lumbar drainage following laminectomy or the insertion of a cannula and rubber drain, lavage, and the administration of various chemical agents or specific and non-specific serums. These latter may be administered by various routes, subcutaneously, intravenously, intraspinally, by the cistern, into the ventricles, or by the carotid. The various measures have been thoroughly reviewed by Tripoli.[7]

The value of any particular method remains a matter of conjecture. Procedures such as cisternal puncture and forced drainage have been shown to be not without danger; sudden death may occur. A similar criticism also applies to the use of certain antiseptic agents; unfortunately a chemical has not yet been discovered that will destroy the streptococci *in situ* and leave the nerve tissue uninjured.

Some hold that intensive treatment of these patients may prove more harmful than beneficial. Certainly, the two patients treated by me who recovered were subjected to a minimum of therapeutic procedures.

Kolmer, who has carried out extensive research on the meningitis resulting from infection with pyogenic cocci, claims to have obtained beneficial results in the treatment of experimental meningitis of the lower animals by administering antiserums and chemical agents by the intra-carotid route. He emphasized that a measure of success was obtained in the treatment of the experimental animal only when such treatment was instituted within 48 hours of the onset of infection. Undoubtedly more success could be expected in the treatment of bacterial meningitis were it possible to institute therapeutic measures within the first 36 hours of invasion.

Treatment early in the disease postulates a diagnosis of the condition in the early stages of invasion. A diffuse, rapidly spreading meningitis readily discloses its presence by the clinical signs and cerebrospinal fluid findings. Not so readily may one determine "meningismus" from a circumscribed area of meningitis or at what moment the latter becomes invasive. I think it is true that in the early stages and when the diagnosis may be in doubt a natural tendency prevails to hesitate before instituting treatment. To make the decision is, in the light of experience with therapeutic results, tantamount to formulating a gloomy or almost hopeless prognosis.

Symptoms of meningitis indicate the necessity for a lumbar puncture and the slow withdrawal of 5 c.c. or less of the fluid for diagnostic purposes. The findings—increased pressure, increased cells over 100 per c.mm., increase of protein, and possibly the presence of streptococci in smear or in culture—may either indicate or determine the presence of a streptococcus meningitis. Whatever therapeutic measures are to be undertaken should be instituted without delay. The immediate administration of specific antiserum is indicated; it may be given by the intra-carotid route. Lumbar taps at 8 or 12 hour intervals are considered advisable, although in the absence of pressure symptoms 24 hour intervals may suffice; the fluid may be slowly drained off until the pressure reaches 4 mm. of mercury. Naturally, stress is placed on the necessity of extirpation of the primary focus or procuring of adequate drainage.

Appended is an abbreviated report of 8 cases.

CASE 1

A boy, aged 6, ill three weeks before entering hospital. Otitis media. Emaciation, marked rigidity of neck; Kernig's sign present. The temperature ranged from 99 to 104°. Hæmolytic streptococci (group A) were found on culture of the spinal fluid. Rabbit serum and human serum was administered at intervals for two weeks, subcutaneously, intravenously, intrathecally, and into the cistern. The boy's condition improved for a time; his temperature fell to normal, and he became bright and cheery, only to revert one week later with severe headache and vomiting. Spinal tapping indicated a block. He died on the 44th day. Autopsy indicated that an abscess of the brain had ruptured into the 4th ventricle. The acute return of symptoms may have a possible explanation in the rupture of the abscess.

CASE 2

A woman, aged 50, was admitted to hospital with septic sore throat associated with œdema of the pharynx. Her temperature was 102°; pulse 110. The following day she developed a severe migraine, rapidly followed by strabismus and diplopia. Cultures of the blood and cerebrospinal fluid taken on the 2nd day were positive for a hæmolytic streptococcus (group A). On the third day the temperature rose to 104°; pulse 160. She became unconscious and died on the 4th day. Treatment: on the 3rd day the patient was given a transfusion of human serum and polyvalent antistreptococcic rabbit serum together with human serum intraspinally. Lumbar drainage was done on the 2nd and 3rd day.

CASE 3

This patient entered hospital on February 13, 1936, with acute otitis media. On February 14th the temperature was 104°. Next day the temperature was 105°; opisthotonos, irregular pupils, stupor. The spinal fluid showed 3,600 cells, globulin xxx, streptococci in smear (on culture hæmolytic, group A). On February 16th, 2 c.c. of rabbit's serum were given together with 10 c.c. human serum intrathecally. On February 17th 2 c.c. of rabbit serum and 30 c.c. of human serum were given intravenously. On February 18th cisternal puncture was done and 2 c.c. and 10 c.c. rabbit serum were given into the cistern. On February 19th serum was administered by vein. A lumbar tap was done twice daily, without improvement. The patient died on February 20th.

CASE 4

An infant girl, aged 4 months, was admitted to hospital following local treatment of a hæmangioma of forehead. Her temperature was 105°. The blood count was 23,000; cerebrospinal fluid pressure was 25 mm. of mercury; 1,700 cells; globulin xx; streptococci were found in the smear (on culture hæmolytic, group A). Treatment: on the 2nd day anti-meningococcic serum was administered intrathecally, and a cisternal and lumbar tap were done each day. On the 4th day her condition rapidly became worse, and 4 c.c. of rabbit serum were administered intramuscularly. She died on the 5th day.

CASE 5

A man, aged 40, had an injury of the frontal bone. He was unconscious when admitted to hospital; temperature 105°; pulse 150. Spinal fluid cells numbered 1,700 per c.mm., globulin xxx; streptococci were present in smear and a hæmolytic form (group A) on culture. A combined inoculation of rabbit serum and human serum was given intra-ventricularly. The patient died within 24 hours of admission to hospital.

CASE 6

A man, aged 50, was admitted to hospital for emergency mastoidectomy; temperature 103°; pulse 100. Blood count gave 22,500 leucocytes, 86 per cent being polymorphonuclears. The patient complained before operation of pressure over the entire skull. Slight strabismus was present. No improvement followed operation; and the headache became more severe. Blood culture and spinal fluid culture on third day showed streptococci (hæmolytic, group A). Meningeal symptoms increased in severity and the patient died on the 5th day. Treatment: spinal taps and one intravenous inoculation of rabbit serum and human serum on the 3rd day.

CASE 7

A woman, aged 34, was admitted to hospital with acute otitis media. Mastoidectomy. The patient's symptoms subsided and she left the hospital, but returned one week later, suffering from an acute onset of a severe migraine associated with vomiting. On admission the temperature was 104°, pulse 140, and the patient was stuporous. Convergent strabismus and opisthotonos were present. The cerebrospinal fluid showed 3,400 cells per c.mm. (90 per cent polymorphonuclears); increase of globulin, and streptococci in smear (hæmolytic, group A, in culture). The patient was given 2 c.c. of anti-streptococcic rabbit serum subcutaneously and 30 c.c. of human serum from a compatible donor intravenously. The following day the general condition was somewhat improved, and 2 c.c. of serum from a previously immunized rabbit which had been inoculated with a vaccine prepared from the causative organism were given intravenously, together with 30 c.c. of human serum. The patient continued rapidly to improve. The following day a further inoculation of the specific rabbit serum was given. Only 1 lumbar tap was made, that for diagnosis. In one week the patient appeared normal and was discharged on the 10th day. For six months she complained of recurring attacks of migraine, but these gradually disappeared and she has remained in normal health.

CASE 8

A woman, aged 32, had a middle turbinectomy with apparent recovery. She was discharged from hospital on the 6th day, but returned four days later with a temperature of 102°, severe headache, chills, and vomiting. Rigidity of neck; Kernig's sign were present. The spinal fluid was under pressure, cloudy, cells 1,300, globulin xxx, streptococcus in smear, hæmolytic in culture. Three c.c. of polyvalent anti-streptococcic rabbit serum were given subcutaneously, and on the following day 25 c.c. of human serum, together with 1 c.c. of rabbit serum intravenously. On the 4th and 5th day 3 c.c. of rabbit serum were given subcutaneously. One spinal tap daily for 5 days. On the 3rd day the patient showed definite improvement, the headache was not so severe, and the rigidity of the neck was less marked. The cells in the spinal fluid fell to 1,090 on the 3rd day, to 840 on the 4th, to 292 on the 5th, when the relation of polymorphonuclears and lymphocytes of the first examination became reversed, now 8 per cent polymorphonuclears and 92 per cent lymphocytes. Headache, rigidity and Kernig's sign disappeared. Her temperature gradually fell and reached normal on the 10th day. She has remained in apparent good health.

COMMENT

The method of treatment with human serum and hyper-immunized rabbit's serum was similar to the method that I have previously described for the treatment of septicæmia.[8] In 4 of the cases the progress of the disease was rapid; sufficient time did not elapse following the isolation of the streptococcus in which to stimulate

the hyper-immunization of the rabbits; at least 40 hours is required.

Treatment with serum was instituted in 3 of the patients within 48 hours of the onset of the meningeal symptoms; 2 of these patients recovered.

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ESSENTIAL THROMBOCYTOPENIC PURPURA HÆMORRHAGICA

(A REPORT OF SIX OPERATIVE CASES)

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NO apology is necessary for presenting six cases of essential thrombocytopenic purpura hæmorrhagica treated by splenectomy since the condition is as yet not clearly understood, and comparatively few cases have been reported in the literature since Paul Kaznelson, in 1916, suggested treatment by splenectomy.

A number of the hæmorrhagic diseases described by the early observers can be classed as essential thrombocytopenic purpura hæmorrhagica, as differentiated from the other forms of purpura, scurvy, etc. "Morbus maculosus", described by Paul Werlhof, (1699-1767), is probably the first attempt to describe this condition as we now know it. Later, in an article on blood clotting, Hayem first described platelets, and in 1889 Denys reported that the condition referred to was characterized by a loss of platelets. Prolongation of the bleeding time was first described by Duke and, as mentioned above, Kaznelson advised splenectomy as the treatment of choice.

These cases may be classed as acute and chronic, and the results of operation vary considerably in the two classes. The cases that come to operation in the latter class usually do well and their post-operative condition remains good; those that are operated upon during an acute exacerbation (to be avoided whenever possible), show a much higher operative mortality, and those patients who do recover are liable to recurrences. Unfortunately many of these cases, when first seen, are in the acute stage, and efforts should be made by transfusions, repeated frequently, iron, hæmostatic sera, x-ray and radium over the spleen to change the picture to one of chronicity. The writer admits that these efforts produced no results in the five acute cases out of the six to be reported. In spite of this the greatly increased mortality should warrant a trial of every possible means towards that end.

Characteristic symptoms are prolonged bleeding time, with normal, or nearly normal, clotting time, a fall in the platelet count, from a normal of 200,000 or 300,000 to a low of 15,000, or less, and what has been described as a "positive capillary resistance test". This is determined by placing a rubber bandage about the arm so as to cut off the venous circulation only. In essential thrombocytopenic purpura a crop of hæmorrhagic spots will appear if the pressure is applied for three minutes. (In the writer's cases this was positive in two, negative in two, and not tried in the other two). Further symptoms, also found in other purpuric conditions, are hæmorrhages from the mucous membranes, into hollow viscera, into the skin, joints and central nervous system. Then one finds severe, sometimes continuous, hæmorrhages from the uterus in women who have menstruated. Following this the usual symptoms of secondary anæmia will be found, and frequently, in the acute cases, there is a rise of temperature.

Sometimes these hæmorrhages are accompanied by severe pain before any visible signs appear, particularly when these are into the joints.

Chronic cases should receive transfusions as a routine before and during operation. We have not noted any beneficial effect from these on the blood picture, but are satisfied that the resistance is improved and operative shock, never severe in our cases, is minimized. If possible septic foci, such as teeth and tonsils, should be attended to, but this is usually difficult because of hæmorrhage.

The operation of splenectomy itself presents no great difficulty, except profuse hæmorrhage, until the splenic pedicle is clamped. Adhesions, however, in the region of the diaphragm may present a most formidable obstacle. Hæmorrhage in all our cases has been severe, but it has been observed that this ceases in a most dramatic manner almost immediately after the spleen is removed.

Of the cases to be reported all but the second were acute, and none of these acute cases improved under treatment and were operated upon in the acute stage. Four of the six have recovered completely; one is very much improved; and the last operated upon is dead. Five or six other patients have been seen by the writer who have not been operated upon, and all have died of hæmorrhage. Here it might be mentioned that three causes are given for failure to obtain cure in these operative cases. The first of these is the presence of accessory spleens, of which three or more have been found in some cases. The second is that in some cases fragments of spleen are left behind while dense adhesions are being freed, and these, as the accessory spleens, will hypertrophy and replace the spleen. The third cause is an involvement of the reticulo-endothelial system which is not clearly understood.

CASE 1

V.R., a girl, aged seven, was first seen in September, 1925, with a history of painful swellings in various parts of her body, which commenced about three weeks before. About twenty areas of hæmorrhage were seen, mostly on the lower limbs. The personal and family history were negative, and, apart from chronically inflamed tonsils and carious teeth, no abnormalities were found.

Treatment was begun with calcium, hæmostatic sera, rest and transfusions. A blood picture was negative, with the exception of the platelets which were 170,000. Within a few days hæmorrhagic areas became almost confluent, and, after complaining of severe abdominal pain, she passed tarry stools and vomited blood. Her platelets had then dropped to 150,000 and her general condition was becoming alarming. On September 17th there were bloody emesis, tarry stools, bloody urine and severe abdominal pain. Her red cells had dropped to 2,700,000 and her platelets to 40,000. On the 19th an emergency splenectomy was done, blood transfusion being given at the same time.

At operation there was little hæmorrhage, the spleen was free and easily removed and was found to be somewhat enlarged. The post-operative course was uneventful, and reference to the accompanying Table will show the blood improvement. Her general condition today is excellent, she has menstruated regularly since the age of thirteen, has had one serious accident attended with average hæmorrhage, and has had her tonsils removed with only the usual precautions. Recently she has been married and is now about four months pregnant and is in perfect health with a platelet count of 273,000.*

TABLE

	Case number, Age and Sex					
	Case 1 Age 7 Female	*Case 2 Age 42 Male*	*Case 3 Age 6 Male*	*Case 4 Age 10 Female*	*Case 5 Age 23 Female*	*Case 6 Age 18 Female*
Lowest pre-operative platelet count.....	40,000	20,000	16,000	20,000	40,000	40,000
Platelet count the day after operation...		93,000	43,000	130,000	170,000	80,000
Platelet count five days after operation..	150,000	270,000	190,000	420,000	213,000	50,000
Platelet count one month after operation	500,000	320,000	242,000	160,000	233,000	Died
R.B.C. the day before operation.....	2,700,000	1,400,000	1,650,000	2,760,000	2,080,000	1,800,000
R.B.C. the day after operation.....		2,080,000	2,100,000	2,680,000		2,200,000
R.B.C. five days after operation.....	3,500,000	3,100,000	2,800,000		2,640,000	1,650,000
R.B.C. one month after operation.....	5,500,000	4,400,000	4,280,000	4,100,000	3,660,000	Died

CASE 2

M.A.S., a railway engineer, aged 42, complained in 1927 of frequent hæmorrhages from his gums, nose and into his skin. The first of these occurred "about three months" before the writer saw him, but they had become so severe that he had done no work for over a month. His previous history was entirely uneventful, and on physical examination the three outstanding points were the perfect physique, the pallor of the skin, and the profusion of hæmorrhagic areas on all parts of the body. Reference to the Table will show the blood findings and,

* Since writing the above this patient has been delivered of a full-term baby with no more than the normal amount of hæmorrhage. Her blood-platelets on the day of confinement were 260,000 and the next day, 320,000. The blood count was normal otherwise.

in addition to these, we had a prolonged bleeding time with a normal clotting time.

In spite of transfusions and other routine treatment this patient did not improve, and splenectomy was undertaken under ether anæsthesia. The removal of the spleen was comparatively easy as there was but one attachment to the diaphragm, and hæmorrhage was not alarming. This spleen also was somewhat enlarged, though this could not be demonstrated before operation. His post-operative course was undisturbed and he returned to his work in about two months. Recent correspondence with this man reveals the fact that he has not lost one day's work through illness since his operation and has had no hæmorrhages.

CASE 3

C.McD., a boy aged 6, was first seen in 1928 with very painful hæmorrhagic swellings of both knees and a history of having had frequent nose bleeding and cutaneous hæmorrhages since infancy. His father had been a patient in a mental hospital since before the boy's birth and also suffered from tuberculosis. The usual large family, often found in these cases of destitution, had fared badly, and the boy had always been undernourished and had been a prey to all the diseases of childhood. Efforts were made to build the boy up and were continued for a period of five months, but each time some improvement was seen it was lost by some new hæmorrhage, until splenectomy was advised and accepted.

In this case hæmorrhage at the time of operation was severe, and the spleen, enlarged, was densely adherent to the diaphragm, from which it had to be freed with scissors, and to the splenic flexure of the large intestine. It was remarked at the time that minute portions of the spleen were left adherent to the diaphragm, and, considering the condition of the child, no apology is necessary for this fact.

The post-operative course was stormy. Several transfusions were given and he left the hospital entirely free of hæmorrhages and having gained some weight. Unfortunately, his home surroundings were most unfavourable and the boy again became under-nourished. There were no further hæmorrhages however for eighteen months, when his old symptoms, bleeding from the nose, into his skin and joints, and from his rectum, returned. These, to date, have never been sufficiently severe to cause any alarm nor to cause loss of time at school.

This case is one which illustrates what will happen when portions of spleen have been left behind and, one might say, was almost expected at the time of operation. Further surgery, or x-ray therapy, has been suggested, but the mother will not give her consent. All that can be done is to watch the boy for later developments and to be prepared to act accordingly.

CASE 4

A.M.H., a girl of ten, was admitted to the hospital on October 26, 1934, with a history of recurrent hæmorrhages, particularly from the nose, for a period of over four years. No diagnosis had been made and previous treatment had been symptomatic, including one transfusion. The parents say that only when hæmorrhages were severe did they seek medical advice, but that minor nasal hæmorrhages were of almost daily occurrence.

On admission she was found to be covered with bruises and petechial hæmorrhages, and blood was present in the stools, (possibly from the nose). Her general condition was poor and her platelet count was 45,000. In spite of two transfusions and general reconstructive treatment the hæmorrhages increased and the platelets fell to 20,000 on November 5th. At that time the coagulation time was two minutes and the bleeding time nine and one-half minutes. The spleen was just palpable, and she was rapidly going down hill.

The following day the spleen was removed, after freeing moderate adhesions to the diaphragm and to the tail of the pancreas. Hæmorrhage was not severe and the abdomen was closed without drainage. That night all hæmorrhages had stopped; the platelet count was 70,000 and two days later it had risen to 210,000. From that time the child has been perfectly well, has had no hæmorrhages of any kind, and a recent platelet count is 230,000.

CASE 5

M.R., aged 23, a school teacher. Was first seen after her admission to hospital on January 22, 1935, with a history of excessive menstruation and epistaxis for a period of about five months. Previous to that her health had been perfect and her family history was negative. She had, in addition to these hæmorrhages, numerous hæmorrhagic spots on her body, particularly on her back, about 1 cm. across. Here again direct transfusion was done, but the hæmorrhages only seemed to be aggravated thereby. Her platelet count was 40,000; her hæmoglobin, 50 per cent; and her red cells, 3,640,000; but her general condition was fair. On the night of January 28th her vaginal hæmorrhage was so severe that a splenectomy was done early the following morning. The spleen, macroscopically, was normal in every way, except that it was adherent to the diaphragm by recent adhesions, which were easily broken down. The abdomen presented no other disease and was closed without drainage.

Twelve hours later the vaginal flow had ceased, the platelets were 150,000, and she expressed herself as feeling very much better than she had done for a long time. She was discharged from the hospital on February 10th and was readmitted on March 15th with an acute gangrenous appendix. Her platelets were then 233,300 and her hæmoglobin, 70 per cent. The red cells were 3,600,000 and her white cells only 2,400. The cæcum was markedly injected and pus was present, but well walled off. The appendix was removed, drainage was instituted, and the patient returned to bed. Two days later, and for the next three days, she passed quantities of blood per rectum but, in spite of that, made an excellent recovery. She is at present back at school, her general health is very satisfactory and she menstruates regularly four days a month. Since her appendicectomy she has had no hæmorrhages and considers herself to be as well as she ever has been.

CASE 6

A powerful farm girl of 18 consulted the writer on December 21, 1935, for hæmorrhages from the mouth, gums, throat and nasopharynx. Her history revealed the fact that, following "a cold" three months before, her menstrual periods, previously normal, had become profuse, and that the present period had started December 1st. For about three months she had noticed frequent hæmorrhagic areas on her lower extremities. Both feet had been swelling and the left looked as if it had been crushed by a steam roller, a regular hæmorrhagic mass to above the ankle. She was weak, listless and nervous, and in very poor condition. Sent to hospital that day, her blood count was found to be hæmoglobin, 28 per cent; red cells, 1,600,000; white cells, 8,800, with a normal differential count; and platelets, 50,000. As donors were available she was immediately transfused three times, with but little result. The hæmorrhages increased and the platelets fell to 40,000 on December 28th. In view of the non-improvement splenectomy was proceeded with that same day. The spleen was found to be considerably enlarged and adherent to the splenic flexure of the colon. Its pedicle was so short that the application of clamps was impossible and it was necessary to ligate it *in situ* before

extirpation. Hæmorrhage was rather free, but was replaced by 500 c.c. of blood on the table, and she was returned to her bed in fair condition. That night her platelets were 90,000 and her condition improved, but the following day the platelet count was falling again. On December 31st she suffered from a very profuse epistaxis, requiring anterior and posterior packing. The following day she became irrational and her general condition began to fail rapidly with copious free hæmorrhages from her nose each time the packing was disturbed. Daily transfusions were given with no result, and she died January 11, 1936. The last blood count, two days before death, showed hæmoglobin 35 per cent; red cells 1,600,000; and platelets 50,000. Unfortunately, it was impossible to secure a post-mortem in this case.

This death, the only one in the series, might have been prevented by deep therapy, which was considered but rejected owing to the possible severe reaction and the loss of time, neither of which she was in a condition to stand. . The question of an accessory spleen must be considered here as we are satisfied that the spleen itself was removed *in toto*.

CONCLUSIONS

This condition is more widespread than one would suspect and the diagnosis lies in the laboratory.

The treatment that is most successful is the removal of the spleen.

Those operated upon usually recover and do well in after life.

Those not operated upon usually die.

Results are better if the operation is done in the "interval" rather than when the case is acute.

Palliative treatment, with the exception of x-ray and radium, is of little value.

ERYTHROCYTE COUNT AND HÆMOGLOBIN PERCENTAGE IN THE BLOOD OF ADULT MALES IN SASKATCHEWAN*

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Saskatoon

TWO years ago we made an investigation into circulatory conditions of the male students at our medical school here. This was carried out during the months of February and March. Only students who appeared healthy in every way were used. We estimated the red cell count with the Neubauer hæmacytometer, the oxygen capacity by Haldane's blood-gas analysis method, and the blood-pressure by the modified Riva-Rocci sphygmomanometer. Red cell counts varied from 5,000,000 to 5,850,000 per c.mm., with an average count of 5,300,000 per c.mm. The oxygen capacity varied from 18.7 to 20.3, with an average of 19.8 c.c. per 100 c.c. of blood. The average blood-pressure at rest was 124 mm. Hg. systolic and 85 mm. Hg. diastolic. The pulse rate at rest averaged 66 per minute. Both the red cell count and the oxygen capacity averaged much lower than we had expected. Considering that the time of the year with low temperatures and hard study might influence the findings we determined to repeat some of the investigation in the summer months. So, during the month of May, 1936, we investigated the red cell count and hæmoglobin percentage of healthy adult males. Some were university teachers and others were out-of-doors workers in the university gardens. We chose only apparently healthy persons. The hæmoglobinometer was checked by comparison with the oxygen capacity of the blood, 18.5 c.c. of oxygen in 100 c.c. of blood corresponding to 100 per cent hæmoglobin. The following Table shows the findings in 20 cases.

TABLE I

Initials	*Age in years*	*Red cell count per c.mm.*	*Percentage of hæmoglobin*	*Colour index*
L.F.	34	5,500,000	115	1.05
C.W.	44	5,500,000	110	1.0
J.F.	54	6,000,000	115	0.96
A.P.	45	5,100,000	101	1.0
C.J.	25	5,350,000	110	1.03
J.J.	46	5,750,000	114	0.99
R.R.	30	5,900,000	117	0.99
A.R.	49	5,700,000	117	1.02
M.R.	20	5,300,000	110	1.037
H.M.	40	5,300,000	111	1.047
H.L.	23	5,700,000	116	1.02
E.T.H.	30	6,060,000	118	0.97
O.B.	32	5,500,000	110	1.00
J.R.	25	5,700,000	115	1.01
B.S.	35	5,790,000	116	1.00
R.C.R.	40	5,550,000	117	1.05
G.B.	20	5,290,000	113	1.07
A.I.	47	5,305,000	111	1.07
J.W.	26	5,000,000	108	1.08
P.R.	48	5,040,000	110	1.09
Average	35½	5,516,750	112.7	1.024

* From the Physiology Department, University of Saskatchewan.

DISCUSSION

It is well known that there are great variations in the erythrocyte count at different ages, under different environments, and in the same individual at different times. Also the count in the capillary blood of the finger or lobe of the ear may differ from that found in the small arterioles and venules. As it is usual for the clinician to use capillary blood from the finger or ear, the blood in our investigation was taken, at all times, from the finger.

For purposes of comparison and to ascertain degrees of anæmia or erythræmia, as well as to find the colour index, some standard must be accepted as a control, both for the erythrocyte count and for the hæmoglobin percentage. The generally accepted one is 5,000,000 red cells per cubic millimetre in males, and 100 per cent hæmoglobin (Haldane) indicates an oxygen capacity of 18.5 c.c. per 100 c.c. of blood. We used the Hellige normal hæmometer, using 1/10 N. HCl, after standardizing it against the findings from Haldane's blood-gas analysis method of finding the oxygen capacity.

When we seek information in textbooks of physiology regarding the normal red cell count we find great variations. For example one well known textbook[1] gives 5,000,000, another[2] gives it as 5,400,000, while a well known text[3] on clinical methods states: "It is commonly 6,000,000 or a little less".

It is generally accepted that both the red cell count and the hæmoglobin increase with increasing altitude, as is seen from the following Table taken from a well-known textbook of physiology.

TABLE II

	Height above sea level in metres	*Red cells per cubic millimetre of blood*
Christiania	0	4,970,000
Zurich	412	5,752,000
Davos	1560	6,551,000
Arosa	1800	7,000,000
Cordilleras	4392	8,000,000

The partial pressure of gases in the atmosphere decreases with the increase in altitude above sea level, till at 5,500 metres it is reduced to nearly one-half. The altitude above sea level of this part of Saskatchewan is approximately 1,700 feet. At this level the partial pressure of oxygen of the air is reduced by about one-twentieth. Instead of being 21 per cent of 760 mm. Hg. or 159 mm. Hg., as at sea level, it is 151 mm. Hg. in this locality.

According to the researches of others this decrease in partial pressure of oxygen should cause a compensatory increase in the red cell count and hæmoglobin. If we use the Table given here this increase will amount to 800,000 per c.mm. Thus if we assume that 5,000,000 red cells is correct at sea level, the number in this part of Saskatchewan should be nearly 5,800,000 per c.mm. This is higher than our average finding. But if we use 6,000,000 as correct for sea level, then we should have here about 6,800,000 per c.mm., a number not nearly approached in our investigations past or present. In none of our cases did the count far exceed 6,000,000 per cubic millimetre. The hæmoglobin percentage also did not rise to corresponding levels.

As we have said we confined our investigations to men in good health, and used reliable instruments, and each subject's blood was examined twice by each of us and the results compared. The findings therefore should be reliable. The relatively low red cell count and hæmoglobin percentage cannot be due to increased fluidity of the blood, for this was tested by the hæmatocrite and found normal. It may be suggested that the long distance from the sea, approximately 1,000 miles, may have an influence. But it is more likely that the trifling lowering of the partial pressure of oxygen, namely 1/20th, is insufficient to require a compensatory rise in hæmoglobin and number of erythrocytes. It is possible that, in spite of the findings of others, the compensatory increase does not begin till the partial pressure of atmospheric gases is still further reduced. In other words the oxygen pressure here, 151 mm. Hg., is quite sufficient to nearly saturate the hæmoglobin of the blood as it does at sea level, and no further increase being necessary the red cell count and hæmoglobin remain at practically the same level as at sea level.

CONCLUSIONS

The red cell count for adult males in this part of Saskatchewan averages 5,500,000 per c.mm., the hæmoglobin averages 113 per cent, and the colour index is therefore 1.02 during the month of May. During the winter months it tends to be a little lower.

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SOME NEW THORACIC SURGICAL INSTRUMENTS

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THE whole backward path of surgery is littered, like the plains of the American desert, with the out-worn and clumsy relics of technical advances. With what pride their sponsors must have introduced these clumsy tools to the astonished gaze of an admiring world! Surgical instruments in use today are a curious collection of the awkward heirlooms of the past, mixed with the new, delicate and efficient tools of contemporary technology. As a general statement, few will deny that many surgical instruments could be vastly improved upon. Taken as a whole, they are far behind the ingenious tools of the modern engineer or mechanic. Curiously enough, this criticism applies almost entirely to jointed or articulated tools. It is only within the past few years of this century that serious attention seems to have been paid to their modelling. On the other hand, some of the knives, chisels, bistouries and saws of the old masters cannot be improved upon for balance, delicacy and efficiency. The scalpel and chisel are in the direct line of descent from the sharpened flint or celt, the saw and file, from the neolithic imitation of the teeth of fish and animals. The great imaginative leap forward was in the application of a cutting or crushing force by indirect action brought about by joints. The evolution of this tremendous idea has been traced among the Gallo-Roman finds in France. (See M. Baudouin, *Arch. Prov. de Chir.*, Paris, 1910, **19**: 228-38). Just as the inventor of the first primitive wheel can be held responsible (and what a responsibility!) for the very mixed blessings of modern machinery, so that unknown genius who hinged together two knives to make the first pair of scissors, is the true father of modern surgical instruments. The mind of the modern inventor, whether it be of automobile accessories, radios, aeroplanes or dish-washing machines, is in tune (perhaps he sets the tune) with the spirit of his time. His dissatisfaction with the old, impatience with slowness and inefficiency, are characteristics of his age. Even variation for its own sake, as an artistic gesture of freedom from conventional design, is quite in the modern manner.

Every new surgical upheaval is immediately followed by a tool wave. This is especially true of the two latest major disturbances—thoracic and neurological surgery. These instruments can be divided roughly into two groups—those of necessity, and those of luxury. It used to be a common saying among the older English surgeons that "only a poor surgeon complained about his instruments". Yet on the other hand, confronted with a certain technical problem, the surgeon has, not infrequently, been baffled in its successful solution merely because of the poverty of his technical equipment. In time, luxuries become necessities.

The instruments and apparatus about to be described are the survivors of as many more again, ill-conceived or immature ideas. They were designed to improve craftmanship, and have been modelled, remodelled and tested over a sufficiently long period of time (most of them from two to five years) to warrant description.

Pneumothorax apparatus. — Some hesitation may be understood in describing another pneumothorax apparatus, since approximately twenty-five machines have been described by Italian, French, German, English, Spanish, and American workers since the time of Forlanini. The truth of the matter is that the injection of air into the pleural space is such a simple affair, mechanically considered, that it lends itself to a large number of possible variations. The requirements of such a machine are that it should be simple, one-man, automatic in action, fool-proof, capable of delivery or aspiration of any desired amount of air at any desired pressure, give constant demonstration of pleural pressures, be light, portable, unbreakable and cheap.

I believe Murphy, of Chicago, was the first to employ the gasometer principle in such an apparatus in the '90's. It was not until three years after making my apparatus that I saw one of these early machines, and I was struck by the similarity of their construction. This, of course, was years before the water-manometer was introduced by Saugman in 1910 and when nitrogen was still being used.

Two transparent jars of unbreakable pyralin are inverted, one inside the other. The outer jar is filled three-quarters full of ordinary tap water. The trapped air is thus under a pressure corresponding to the weight of the inverted inner jar. This has been fixed, arbitrarily, at plus 10 c.c. of water, as a working head of pressure. It can be varied easily by lifting up the inner jar with two fingers, so that a negative pressure of minus 15 c.c. or lower can be obtained, or by pressing down with one finger, so that positive pressure up to plus 20 c.c. is obtainable. In practice, with routine refills, this adjustment is not necessary and the delivery of air is automatic. Only on aspirating air, or for high positive pressure refills, is it necessary to touch any part of the machine, except to turn the tap. For initial injections, the inner jar is run down until the enclosed air is at zero pressure. Two hundred c.c. of air can be sucked into the pleural cavity by virtue of its own negative pressure. There is only one tap to manage. This controls the air flow from the jar to the needle. The water manometer has no tap and cannot be cut off, and registers at all times one of three possible pressures. (1) When the tap is "off" the manometer registers the pressure at the point of the needle. (2) When the tap is "on" and the air is flowing from an unobstructed needle it registers an intermediate pressure between the pressure at the point of the needle, and the head of pressure of the air in the jar. (3) When the tap is "on" but air is not flowing, owing to needle obstruction, it registers the head pressure in the jar only.

In practice the dampened manometric fluctuations show the needle is in the pleural space, even when air is flowing. When the tap is off these fluctuations immediately fall in total pressure, but increase in swing and show at once the true intra-pleural pressure. Both ends of the manometer are protected by small valves which cut off automatically wide excursions in either direction of the water column, such as are produced by coughing or very high or low pleural pressures. These valves drop back of their own weight when the pressure causing them to close is relaxed.

The manometer scale is marked in "true" pressures of c.c. of water, not in half-pressures only, as in so many machines. The capacity of the inner jar is 700 c.c. of air. To recharge, close the tap and simply lift the jar clear of the water, then lower it until it rests on the surface again. At the end of each day pour the water out of the apparatus and refill with tap water when needed. The height of the apparatus is 14½ inches; diameter of outer cylinder, 3⅞ inches; weight without case or water, 3 lbs.; weight with case and without water, 6½ lbs.

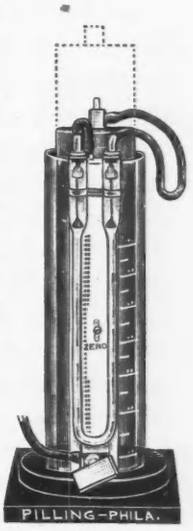


Fig. 1. Pneumothorax apparatus.

Combined pneumothorax and pleural fluid aspirator.—The advantages of such a combined apparatus are obvious and need not be enlarged upon. The same pneumothorax apparatus (1) is used. The vacuum jar of the aspirator is made of unbreakable pyralin, with a capacity of 2,500 c.c. It is easily detachable and is sterilized with cold 5 per cent lysol solution. There is no connection between the vacuum jar and the pneumothorax apparatus. For convenience they are made to sit, side by side, on the same aluminum base, with an instrument board between them containing (1) a pneumothorax apparatus tap; (2) a manometer for pneumothorax; (3) an air filler and fluid trap for protection of the pneumothorax apparatus; (4) a gauge indicating negative pressure in the vacuum jar. There are two tubes leading from, and one tube leading to, the combined apparatus. Of the two outgoing tubes, one is for air from the pneumothorax apparatus to the needle, and the other is for air aspirated from the vacuum jar by the foot pump. The ingoing tube leads from the needle to the vacuum jar and is for fluid or pus. The gauge shows at a glance the negative pressure in the vacuum aspirating jar. It is calibrated from 1 to 30 in

inches of mercury. Knowledge of this negative pressure is essential in safe aspiration of fluid or pus in a "closed" pleural space, to avoid dangerously low pressures. The lid of the aspirating jar is made air-tight by a simple counter-acting thumb screw.

In the operation of aspiration of pleural fluid or air replacement, such as in diagnostic pneumothorax, we aspirate, say 200 c.c. of fluid, at any desired negative pressure, say, 10 inches of mercury, and replace with an equal or lesser amount of air. This operation is repeated until all the fluid is aspirated. One needle (with plunger), and two side outlets (one for the outgoing pus tube, and one for the ingoing air tube), may be used, or one needle (with plunger), and one side outlet only. In the last case the pus tube and the air tube must be switched on the single outlet. The other alternative is two needles—one for the outgoing pus, and the other for the incoming air, separated from each other by several interspaces.

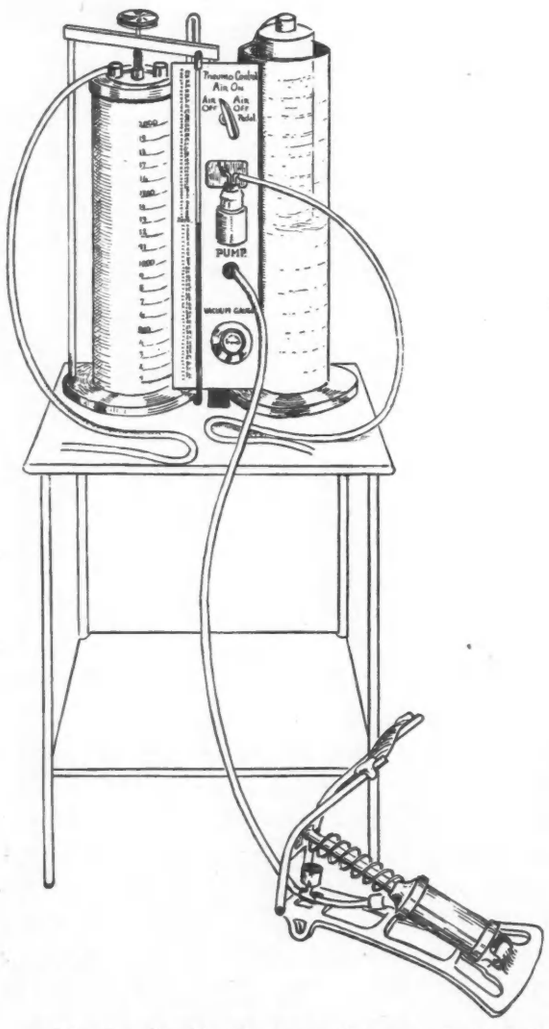


Fig. 2.—Combined pneumothorax and pleural fluid aspirator with foot-pump.

The important things are: (1) use 16 gauge needles or larger for pus; (2) always use a needle equipped with plunger or stilette. Nothing is more annoying than to have a pus needle plug with fibrin, and to be continually detaching the rubber tube to clear it.

We use this apparatus for empyema or large pleural effusions of 1,000 c.c. or more. One may start with a zero pressure in the vacuum jar and obtain any desired negative pressure up to 20 inches. Incidentally, the extremely low negative pressure obtainable on aspiration with a Luer glass syringe of 20 or 30 c.c. size is often not appreciated. Minus 20 inches of mercury negative pressure can be obtained! One is never afraid of losing the partial vacuum in the aspirating jar as it is so quickly regained with one or two strokes of the foot pump. One always knows what negative pressure there is in the aspirating jar. It was on account of this lack of definite knowledge of negative pressure, and of the slowness of obtaining the partial vacuum, which induced us to discard Potain's aspirator.

An aspirating foot pump.—This pump is placed on the floor beside the bed and is operated by pressure of the foot. One stroke gives about five inches of partial vacuum, equivalent to about ten strokes of a Potain's aspirator, using a 2,000 to 3,000 c.c. vacuum jar or Winchester. The gauge on the pump informs the operator at all times of the negative pressure in the jar. The pump is strong and sturdy and the original model was made for me in England by a well-known Sheffield firm of pump makers. For those who still wish to use the ordinary large Winchester as an aspirating jar the gauge has been built into the pump. It is called in our hospital, "The Nurses' Friend".

A self-retaining scapula lifter and retractor.—This instrument lifts and holds the scapula up and forwards, off the chest wall, during an upper stage thoracoplasty. A really extraordinary range of movement is obtained by three universal ball and socket joints, operated by two turnscrews. It can be taken apart in three pieces, and is completely sterilizable, either by boiling or by autoclave. We use the

latter method. It consists of an "arm", a "fore-arm", and a "hand". The joints are the "shoulder", the "elbow", and the "wrist". The shoulder joint has a short, thick, square pin which fits into a socket on the table. All three joints are operated by the assistant from the "elbow", by two turnscrews. This instrument is swung out of the field of operation when not needed. Two or three turns of the screws fix, independently, the wrist and the clawed hand, the elbow and fore-arm, the shoulder and arm. To operate, place the clawed hand beneath the scapula, lift the fore-arm up, pull back the arm, and tighten both screws. It will then "stay put" in the desired position. It will do what an assistant cannot do, willing as he may be, that is, maintain a steady lift and retraction. It is lift and not retraction (this last only pulling the patient forward on his face, out of position) that is desired in an upper stage thoracoplasty. Even with cutting or separation of the upper three digitations of the serratus magnus, as is the routine in this clinic, the self-retaining lifter is still a boon, and, more so, if they are not cut, as in some clinics. It is necessary to point out that the socket attachment receiving the lower end of the arm must be bolted firmly to the table. Otherwise a movement of give or sway will occur between the socket attachment and the table which will render the whole instrument worse than useless. This socket attachment needs only a thumb screw to hold the instrument in it, as a turning movement is prevented by making the pin square and not round. The socket attachment can be made and bolted on the table by any skilled local mechanic. To look well, it should be nickeled, and one fixed on each side of the table at a distance of one foot from the top end. A socket for the chest rest should be bolted six inches below it (see Fig. 3). This instrument was invented because its originator acted for one year as second assistant, with the job of scapula retractor. Of the operating team he was the one who was the most fatigued at the end of an operation. The original model has been altered within the past year to one with larger ball and socket joints, so that the total area of friction is increased. It will now hold in any position a weight of 50 lbs. This instrument has been in constant use for the past five years and is extremely satisfactory. The exposure it gives of the first rib is a new experience to those surgeons who have been accustomed to manual retraction. In no case has the patient complained after the operation of pain in the shoulder, nor has any instance of brachial plexus injury been observed. On reflection, it will be seen that the plexus is actually relaxed by such steady lift-retraction. In our clinic it is called "The Iron Intern".

Two adjustable chest rests. — Metal arms carry hinged, slightly curved wooden boards which serve as rests for the chest. One rest is for the front, the other for the back. They only differ in their width. The front rest is covered with an ordinary pillow, and the back rest has a rounded sausage-like pillow between it and the body. The upright pin, at right angles to the horizontal arm, fits into a socket bolted to the table, 18 inches from the top end on each side. A broad strap across the hips, a pillow between the flexed knees, and one under the head, and the patient is ready for operation.

Rib cutters (two models).—Rib shears were the first thoracic surgical instrument which aroused my dissatisfaction six years ago. There were then four models with which I was familiar—the Doyen, the Gluck, the Liston, and the double action Liston. All seemed to me to possess some fault, either the too-sharp points, the short handles, or their heaviness and general clumsiness. I do not include the special first rib shears of Sauerbruch, Lilienthal or Stille, the last of which is still a great favourite of mine and one which I think cannot be improved upon for cutting the posterior end of the first rib.

My original model of 1928 was a copy of a leather-cutting shears made by the United Shoe Machinery Company. The only alteration made was to blunt the points. Two years later it was remodelled, using a stiffer steel (the first was too flexible), and putting rubber grips on the handles. For ordinary use it is still my favourite. The ratio of jaws to handle length is 3.5 cm. to 29.5 cm. This gives tremendous leverage; most ribs can be cut with one hand. It is as powerful as a double-action shears and is lighter and more graceful in manipulation. (Fig. 4). It takes the hard work out of rib work.

For cutting the anterior ends of the ribs in the modern complete costectomy the jaws were angulated more in the second model. Since then Welles and Meyer introduced (1933) even more sharply angulated-jawed cutters, which seem to me to be very useful for cutting the anterior ends of the ribs. Only one posterior section is made of any rib in our technique. This section includes the transverse process of the vertebra. (We abandoned the Sauerbruch technique of double posterior section several years ago, as time-consuming, without compensating in improved results.)

In about 50 per cent of cases the anterior end of the first rib, after the separation of the anterior scalene muscle from Lisfranc's tubercle, can be twisted out easily, the chondrocostal junction of the rib breaking through edge. This facilitates its introduction between the periosteum and the rib. Since the leading edge of the jaws is sharp, it is a "pusher" stripper. The first assistant, who stands above the operator on the same side of the table, strips the upper edge of the rib from behind forward. He then hands the stripper to the second assistant, standing opposite, who then strips the lower edge of the rib from in front backwards. The Doyen stripper is used only very rarely by us. The stripper described is very useful also in clearing off the muscular and ligamentous attachments to the posterior ends of the ribs about its angle and off the transverse process (Fig. 5).

Periosteum scrapers (two models). — These are modifications of two scrapers which have been used by Dr. Archibald, of the Royal

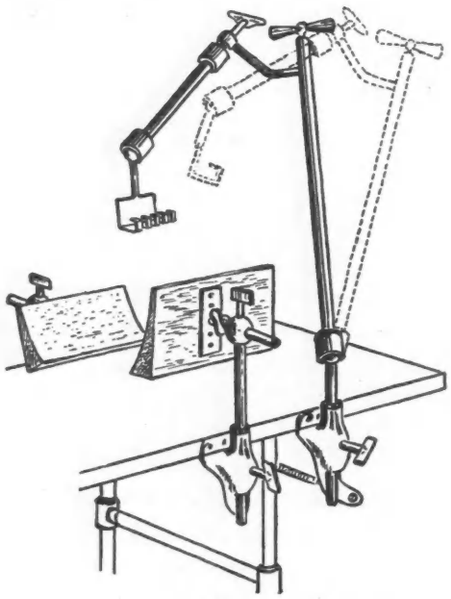


Fig. 3

Fig. 4

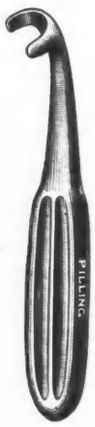


Fig. 5

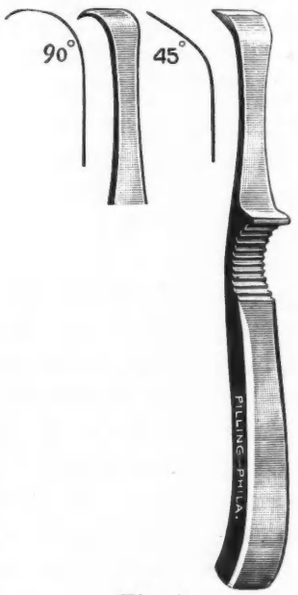


Fig. 6

Fig. 3.—Self-retaining scapula lifter. Adjustable chest rests — front and back. **Fig. 4.** — Rib cutter. **Fig. 5.**—Rib stripper. **Fig. 6.**—Periosteum scrapers.

like a piece of cheese. If it has to be cut, I prefer an angulated shears, such as my second model, or the Welles or Meyer. The brachial plexus and subclavian vein are held away with a retractor.

Rib enucleator or stripper.—I was very much taken with the ingenious Matson-Plenk stripper some years ago. I have modified it to suit my own particular fancy. The jaws have been shortened and the angle between them reduced. A cutting edge forward has been added and the jaws twisted so that the trailing edge is now at an angle of 45 degrees to the leading

Victoria Hospital, for the past twenty years. I believe they are Faraboef's, originally. One has its "beak" set at an angle of 45 degrees and the other at 90 degrees—called by us "the 45" and "the 90". The former is a universally applicable model, the latter, for the first rib. The original handles have been reshaped and lengthened (most scraper handles are too short), and finger rests added. "The 45" is sharp, "the 90", half-sharp. Blunt scrapers are as dangerous as blunt knives (Fig. 6).

Lobectomy tourniquet.—This tourniquet may

be slipped over the liberated lobe as a loop, or with one free end pulled below and up, and tied. The action of closure of the loop is quick and steady and needs only one hand. The cord is of strong, braided, non-stretchable cotton. To loosen the loop the catch on the rack is depressed. We use two of these tourniquets in a lobectomy, and cut between them to prevent soiling the pleura. We have designed three different models of tourniquets in the past three years, and this would seem to be the best. Although quite efficient, my own feeling is that it could be improved upon (Fig. 7).

A set of five phrenicectomy instruments.—These consist of three retractors, a hook, and an avulser. The three retractors have blades of the following lengths: 1st (the operator's) 2 cm.; 2nd (the assistant's) 2.5 cm.; 3rd (the assistant's) 3 cm. The handles are light and short, with engine-turned surface. The blades are set at the angles which we have found most suitable, but can be bent to will. The third retractor is included for those cases which have extra-deep necks. Even in the ordinary case, for the assistant to use two retractors to the operator's one gives a better exposure. There is a perforation in the top centre of the blade of the assistant's retractors, to admit the tip of the avulser. This steadies the forceps and gives it a fulcrum as it twists the nerve out. The hook picks the nerve up off the muscle. The avulser has the guard or shoulder on the lower jaw only. Other avulsing forceps have a split guard divided between the two jaws. The lower jaw, being unencumbered, can be slipped easily under the nerve. When closed and the nerve cut above, the tip of the avulser is lifted slightly and introduced into the hole in the assistant's retractor and can then be rotated without slipping (Fig. 8).

Lung expansion recorder and chart.—This is to take the place of the ordinarily used Wolff's blow bottles after empyema operations. The idea is that the patient keeps a graphic record of his exertions and is thus encouraged to persist. It is a home-made instrument. Take a Tycos sphygmomanometer, and attach a short length of rubber tube with a glass or vulcanite mouth piece. Insert between the mouth piece and the manometer an air filter filled with absorbent cotton. The patient is given a chart marked off in days and pressures, with a horizontal red line drawn across—his "par of expansion". The average par on a Tycos is about 100. He keeps his own score. Day by day he tries blowing to reach "par", and as his lung expands, his capacity increases. The chart is really a record of his intra-bronchial pressure.

Fig. 7

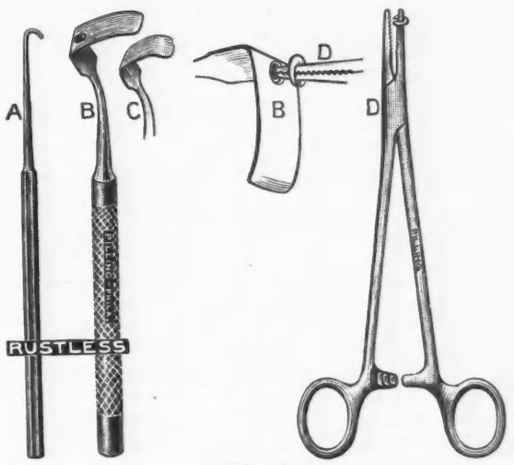


Fig. 8

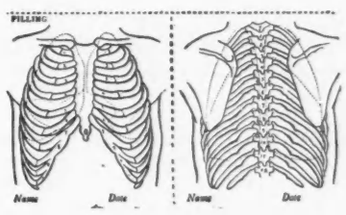


Fig. 9

Fig. 10

Fig. 7.—Lobectomy tourniquet. **Fig. 8.**—Phrenicectomy retractors, hook and avulser. **Fig. 9.**—Sticker chest chart. **Fig. 10.**—Intercostal trochar and cannula.

Sticker chest charts.—These are for the clinician to carry about with him, to record physical findings or fluroscopic recordings, in a sort of short-hand. They are like large postage stamps, with mucilage on one side. They are torn out of the book of 50, moistened, and stuck on the patient's case record or skiagram. A dozen or more can be put on one sheet of paper. The charts come in pairs of "front" and "back" (Fig. 9).

An oval intercostal trocar and cannula.—This

was originally intended, and was used, for the introduction of pleural scissors, clip applicators, and trans-illuminator. Dr. Milton Lloyd, of New York City, has utilized it for introducing a two-way rubber empyema tube for closed drainage (*J. Thoracic Surg.*, 1933, **2**: 302). I think the handle of the trocar should be larger and longer (Fig. 10).

Pilling and Sons Company, of Philadelphia, Pa., are the makers of most of these intruments.

Confessional note.—I have abandoned the use of the following instruments:

1. An air-tight pneumatic empyema tube, made in 1931 but not described. I was not able to prevent it being punctured by the cut ends of the rib.

2. A combined aspirator and pneumothorax apparatus described in the *Canad. M. Ass. J.* (1929, **20**: 663). Its whole conception was shortly seen to be basically unsound. Fortunately, only one was made.

3. The squeeze tap, suspension arm, and glass cylinder of early models of the pneumothorax apparatus, introduced, but not described, in 1928, 1929, and 1930. The glass cylinders were abandoned because they broke; the squeeze tap, because, being attached to the needle, it was necessary, yet difficult, to sterilize; and the suspension arm, because it was unnecessary.

4. A phrenicectomy necklace described in the *Am. Rev. of Tuberculosis* (1932, **26**: 3), was abandoned as unnecessary. It was taken, as it was meant to be, as an amusing little trinket.

5. A lipiodol oil gun described in the *Canad. M. Ass. J.* (1929, **20**: 286), was abandoned as having no great advantage over an ordinary 30 c.c. Luer syringe.

6. Silver clips and applicator, described in the *J. of Thoracic Surg.* (1933, **2**: 302), were discarded in favour of electro-coagulation.

7. A pleural transilluminator, described in the *J. of Thoracic Surg.* (1933, **2**: 302), was discarded in favour of Mauer's cock-up illuminated probe, which is very much better.

Case Reports

A WOUND OF THE HEART WITH FRAGMENT OF STEEL RETAINED IN THE MYOCARDIUM

BY FREDERICK J. TEES, B.A., M.D., F.R.C.S.(C.)

Montreal

"There . . . Alkathoos was slain . . . when the hero Idomeneus smote him in the midst of the breast with the spear . . . and he fell with a crash and the lance fixed in his heart, that, still beating, shook the butt-end of the spear." Thus does Homer describe the first recorded wound of the heart.

Rudolph Matas, in his summary of the history of the surgery of the heart, quotes Sherman as saying: "The road to the heart is only two or three centimetres in length in a direct line, but it has taken surgery nearly twenty-four centuries to travel it." Up to comparatively recent times wounds of the heart were considered to be hopelessly fatal. George Fischer's monumental work, published in 1868, summarized the knowledge then available and suggested surgical approach to the heart as a remote possibility. The famous Billroth is quoted as saying in 1883 that "the surgeon who should attempt to suture a wound of the heart would lose the respect of his colleagues." Sir Stephen Paget, writing in 1896, says: "Surgery of the heart has probably reached the limits set by nature to all surgery; no new method and no new discovery can overcome the natural difficulties that attend a wound of the heart. It is true that 'heart suture' has been vaguely proposed as a possible procedure and has been done on animals, but I cannot find that it has ever been attempted in practice." The rashness of attempting thus to limit the scope of surgery is apparent when it is recalled that in that very year Rehn, of Frankfort, successfully sutured a wound of the human heart.

Since that time with constantly improving methods, "the heart", as Matas says, "has become a surgical organ, and is subject to the same laws and technical procedures which govern the interventions of surgery in the treatment of the injuries and traumatisms of all the hollow viscera." With the passage of time, too,

the tolerance of the heart for foreign bodies has become more and more realized.

The experiences of the war added enormously to the store of knowledge with respect to heart injuries. Matas, in 1922, reviewed the literature of the French, English, Italian and German literature, and has a very valuable chapter on the prognosis and indications for the late or delayed extraction of retained projectiles and other foreign bodies in the heart. It reveals a very great divergence of opinion as to the treatment to be recommended, operative or expectant.

The following case is reported because it illustrates some of the difficulties in this connection.

E.M., a robust young man, 28 years of age, sustained an unusual injury on July 26, 1934. While seated on the ground holding a steel drill which was being struck by a heavy sledge he felt a sudden sharp pain in the left side of the chest. He put his hand inside his shirt and noticed that his fingers were stained with blood. He felt faint but was kept from falling over by his mate who came to his support. He was promptly taken by train and ambulance to Ottawa, a distance of some fifty miles, where he was admitted to hospital. On admission he gave evidence of considerable shock, from which he rapidly recovered under rest. A small wound was noted in the second left interspace, three inches from the mid line. This healed without reaction.

During the three weeks he remained in hospital he developed a moderate rise in temperature and had considerable pain in the region of his heart. His pulse averaged about 100. Radiological examination of his chest revealed the presence of a small metallic foreign body, evidently a fragment from the steel drill or sledge, lying within the shadow of the apex of the heart. This was thought to be in the wall of the pericardium.

Following his discharge from hospital he began to move about quietly, but continued to suffer from periodic attacks of pain in the region of the heart. These varied in frequency, in duration and in intensity. At times he was quite free from symptoms. He found that lying on his face invariably induced the pain. On October 12th, the pain persisted for twelve hours, and two weeks later he had an attack of great intensity lasting about five minutes, during which he became dizzy and very weak. He thought he was going to faint but did not actually lose consciousness. The pain and dizziness continuing, he was referred to me on November 14th. Under fluoroscopic examination at the Western Division of the Montreal General Hospital the foreign body was plainly visible both in the antero-posterior and lateral views. A small fragment the size of a split pea was seen to move tumultuously with the contractions of the heart. Films were made to aid in the localization. The fragment was seen to lie in the shadow of the left fifth rib, three inches from the mid line, three inches from the nipple and four and one-quarter inches below the point of entrance. It was about an inch above the rounded margin of the apex of the heart, and appeared to lie at a depth of about one and one-half inches from the skin surface. Dr. J. MacKay, assistant roentgenologist to the hospital, was under the impression that the fragment lay either in the wall of the pericardium or on the surface of the heart. The peculiar pains of which he complained when lying prone seemed to give support to this possibility. One anomalous finding, definitely established during the fluoroscopic examination, was that the heart shadow together with the foreign body occupied a slightly higher position when the patient was standing than when lying on his back. It is possible that when he was erect the contraction of his powerful abdominal muscles contributed to this difference.

The patient was very anxious to get relief from his recurring pains and entered the hospital for an exploratory operation. During the period of preliminary observation he had a subnormal temperature, 96 to 98°, his pulse ranging from 72 to 92 when recumbent, respirations, 20. The blood pressure reading was 156/85.

Operation was undertaken on November 21st, under intratracheal ether. Drs. C. C. Birchard, C. R. Bourne, and W. W. Eakin cooperated in securing electrocardiographic tracings of the heart action from the beginning to the end of the operation, by leads from the operating room on the tenth floor to the instrument in the basement. The results of this will be referred to later.

There was a choice of two methods of approach to the heart — lateral (transpleural) and medio-sternal (extrapleural). The latter with a transverse division of the sternum above and a central vertical section in the mid line below permits by retraction the exposure of the anterior mediastinum. This undoubtedly gives a better approach to the heart as a whole, and seeks to avoid opening the pleural cavity. The alternative was a lateral exposure. In this the pleura is of necessity freely opened. Formerly the risks of an acute surgical pneumothorax were considered very grave but these are now minimized. The location of the foreign body behind the fifth rib suggested that the lateral exposure would give the more direct approach. Hence an incision was made down the left border of the sternum to the fifth costal cartilage then following the cartilage and rib to the left. Some four inches of cartilage and rib were removed, and the third and fourth costal cartilages were divided close to the sternum. The chest cavity was opened along the course of the incision and the freed ribs retracted upwards. This opened the pleura and exposed the underlying part of the pericardium. At this step the heart shifted somewhat to the right and at a later stage a portion of the sternum opposite the fourth and fifth cartilages was removed by rongeur forceps to give better access. With the opening of the pleura the lung visibly collapsed in spite of the positive pressure of the intratracheal anæsthesia. Large moist towels were placed in the pleural cavity for protection.

A most careful search by inspection and palpation was made in the fatty extrapericardial tissues of the mediastinum for evidence of the fragment but without success. The surface of the pericardium was similarly palpated with like results. Two traction sutures were then placed in the pericardium to steady it and a short vertical incision between the sutures allowed the edges to be held apart. On opening the pericardial cavity a considerable quantity of semi-gelatinous material gushed out. It was of a definitely brown colour, suggestive of old blood pigment, and was under obvious tension. A finger was inserted into the opening of the pericardium but no rough fragment could be felt on the inner side of the sac. Nothing abnormal could be felt on the surface of the heart during this preliminary examination, the convulsive movements making palpation extremely difficult.

The opening in the pericardium was thereupon enlarged to give better exposure. This enabled the sac to be more fully explored, again with negative results. To steady the heart and permit its scrutiny a stay suture was placed through the apex. This controlled the heart sufficiently to reveal a small whitish scar on the surface of the right ventricle about one inch from the apex, in immediate proximity to the left coronary artery, and close to some of its lateral branches. Palpation confirmed the presence of a small depression at the bottom of which could be felt a small firm nodule, the offending fragment beyond a doubt. During the periods

of traction on the heart it seemed to miss several beats, but these apparent cessations were not recorded by the electrocardiograph.

The temptation was very great to incise through the scar and remove the fragment. The major part of the operation over, such a move seemed a simple one. Two considerations weighed in the decision against interference. First, the relation of the fragment to the coronary artery. An incision would have required suturing and it was apparent that the placing of sutures would in all likelihood interfere with the circulation in the artery. The second was the known tolerance of the myocardium for small steel fragments as was proved by the war experiences in all countries. Here was a small fragment embedded and apparently well encapsulated. Was not the hazard greater to remove than to leave the coveted object? So it was decided. The pericardium was closed with plain catgut, the third and fourth costal cartilages fixed to the sternum with kangaroo tendon, the pleural cavity tightly sealed, and the skin sutured.

The wound healed kindly, the collapsed lung refilled promptly, and there was no return of the cardiac pain. The patient was allowed up in a chair on the twentieth day, but resumed his bed the next day on account of the onset of a septic sore throat, accompanied by an irritative cough, which caused us some concern. He was examined by Dr. D. Grant Campbell who reported on December 20th, as follows: "Examination of chest today shows no sign of pulmonary involvement, the lungs being clear on percussion and auscultation. The throat is still slightly injected and the tonsils inflamed. The cough I consider as entirely due to a laryngitis." His improvement continued and he was discharged from hospital on January 6, 1935, quite free from symptoms. He gradually resumed activity and was able to enjoy skiing before the end of the winter. In June he assisted in the building of a barn at his home and during the course of the summer he returned to work as a railway trainman. It would appear that the relief of pressure within the pericardium goes to explain his improvement. As noted above, the viscid contents of the sac were under considerable tension, which doubtless acted as a tamponnade.

The results of the electrocardiographic tracings taken at the time of the operation and subsequently, as reported through the courtesy of Dr. C. C. Birchard and Dr. C. R. Bourne, are given below. For their great interest and cooperation I wish to express my appreciation.

COMMENT

Electrographic records made during the pericardiotomy were to some extent unsatisfactory. The instrument then available at the Western Division of the Hospital was a very early English Cambridge machine, on which extensive repairs had just been completed. Fortunately, it used bromide recording paper, which allowed of lengthy records being made. The instrument being located ten floors below the operating room inter-communication was by telephone only, and this necessitated an assistant in the operating room keeping a log to minutes and seconds for subsequent comparison with the time various portions of the electrographic record were made. This assistant, though an internist, became too engrossed in the surgical technique to make frequent entries in the log, with resulting difficulty in identifying certain parts of the record with the steps of the operation. While

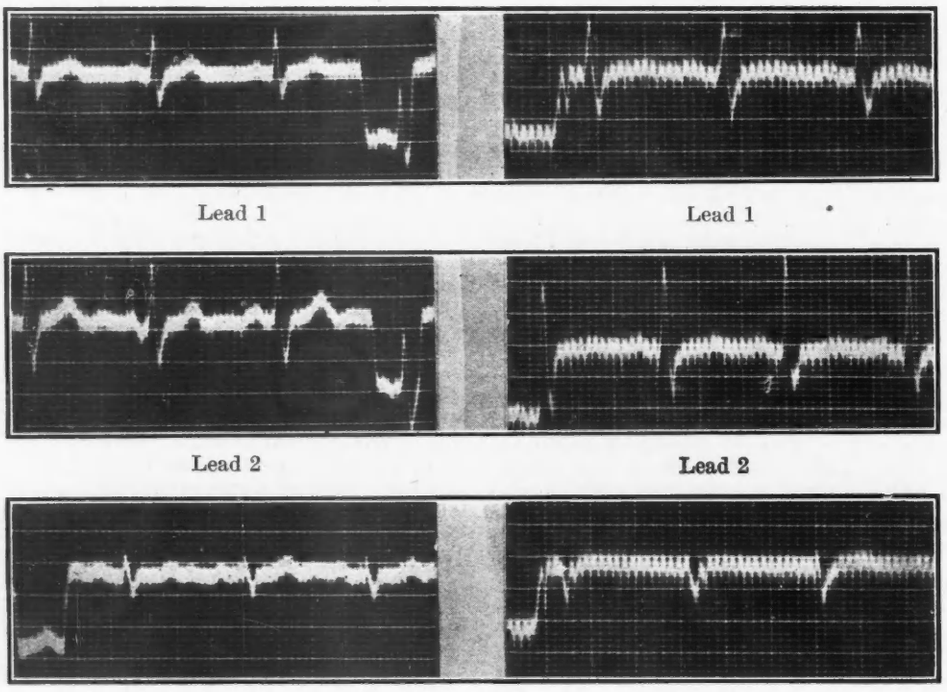


Fig. 1

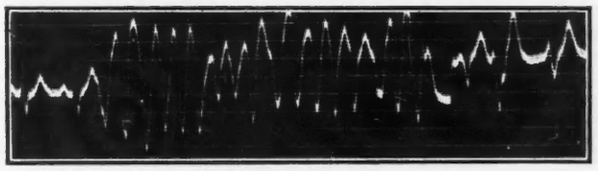
November 21, 1934 (No. 147)
Records made immediately prior to operation.

January 5, 1935 (No. 216)
Record made 6 weeks after operation.

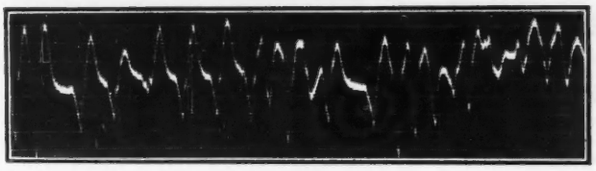
the records were not completely continuous, the shadow of the string was under scrutiny all the time so that gross changes in rhythm could not readily escape detection.

An electrogram immediately prior to operation, Fig. 1 left (three leads) shows a normal record for a patient of this age. Other records made during the early stages of the operation were in no way significantly different.

When the pericardium had been opened, and the heart was being manipulated, the electrographic record showed periods of idio-ventricular



Heart manipulated.



Stay ligatures inserted.

Fig. 2

rhythm alternating with periods of normal sino-auriculo-ventricular mechanism. This is shown in the first graph of Fig. 2. With the insertion of the stay ligature in the apex, rapid irregular idio-ventricular rhythm developed and persisted till the stay ligature was removed. This is shown in the second graph of Fig. 2.

The statement that rapid irregular ventricular rhythm persisted as long as the stay ligature was in place requires some comment, since it appears to be at variance with the surgeon's observation of intervals of cardiac standstill. This apparent conflict of evidence is not necessarily real. The electro-chemical activities of the myocardium need not be associated with actual visible mechanical contraction. Dying hearts in experimental animals have been observed to produce electrocardiograms with the ventricular deflections approximating the normal after all visible mechanical contraction had ceased, and in patients such electrocardiograms have been recorded in this hospital as long as twenty minutes after death. Accordingly it appears possible that during the periods of apparent cardiac standstill observed by the surgeon, the electro-chemical activities of the myocardium were proceeding without associated detectable mechanical responses.

Another hyopthesis is that the periods of apparent standstill were at those times when the tachycardia reached its highest, around 320 per minute. With a tachycardia of such degree the duration of a single cycle is rather less than 0.2 second, much less than the shortest possible duration of a complete ventricular systole. Accordingly the ventricles must have been partly in systole and partly in diastole at every instant during such periods. This is a state of affairs in which a ventricle must practically cease to be a contracting chamber, and to the hand of the surgeon it might well appear to be in a state of standstill.

During the periods of combined arrhythmia and tachycardia, the rate varied from 320 per minute, with a modal rate of around 180 to 200 per minute and the records showed ventricular deflections only. In other words, the cardiac cycles were ventricular extra systoles and apparently arising in more than one focus. An alternative interpretation would be ventricular fibrillation. Whether this or the former is a matter for speculation, but, having in mind that the phenomenon appeared with the insertion of the stay ligature and disappeared promptly with its removal, it appears probable that each cycle originated in the injured area as an extra systole, *i.e.*, the mechanism was one of paroxysmal ventricular tachycardia. Since the injury produced by the ligature was of considerable extent, the points of entry and exit of the ligature in the apex being perhaps an inch apart, extra systoles arising in different places along the line of injury would account for the arrhythmia and the variations in the graphs of succeeding cycles. When the stay ligature was removed the rhythm became regular, with the electrograms not significantly different from those obtained before the operation. Subsequent records, Fig. 1 (right half) showed some diminution in the amplitude of the T-waves, and records of a still later date showed a return of the T-waves to normal magnitude.

AN UNUSUAL CASE OF EMBOLISM

BY W. T. GEMMELL,

Stratford, Ont.

The case I am reporting has been of great interest to myself and all the members of the Staff of the Stratford General Hospital who followed its course. I am especially grateful to Dr. David Smith who helped me throughout its course, and to Dr. Dewitt Wilcox, of London, who came over several times to see the patient, and drove seventy miles after ten o'clock to assist in the post-mortem.

CASE REPORT

Mrs. F.W.H., a well nourished woman of thirty years, mother of three healthy children, was confined on March 1, 1936. Labour was severe, requiring three doses of morphine and hyoscine. Low forceps delivery was employed, and one ampoule of ergot was given after delivery. She vomited during the whole thirty hours of her labour, and continued to do so after delivery until controlled by luminal-sodium by mouth. This vomiting was the only sign of any toxic condition. Her pregnancy had been normal throughout, and no albumin had been found in the urine.

On March 4th I was called, as she complained of numbness in her left hand. I found her hand pale and her nails blue and cyanotic like those of a corpse. No

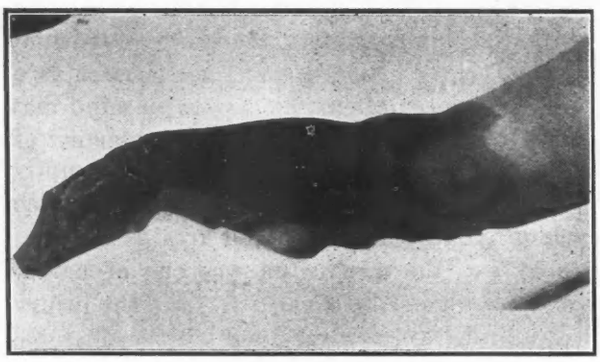


Fig. 1

radial pulse; she could use her hand, and tactile and other sensations were normal, except for the numbness. Next morning she had not slept for pain in her arm and hand, which were now purple and insensitive; she could not use her hand at all. Pin pricks could not be felt up to two inches below the elbow. She was ordered to the hospital. Heart and lungs were normal at this time.

On March 7th the hand was becoming dry, and the purplish discoloration was extending up the posterior surface towards the axilla. A mass could be palpated along the course of the brachial vessels up into the axilla. The outer and anterior surfaces remained white. Immediate operation was considered to check the spread upwards, but after consultation with Dr. David Smith it was decided that she was too ill to stand any operation.

On March 8th her temperature, which had been not higher than 100°, now rose to 105°. Examination of the chest in front (patient too ill to move) showed normal breath sounds and resonance. The heart sounds were normal and the heart was not enlarged or displaced, but the sounds were exaggerated over the whole left chest. A definite cyanosis could be observed over the head and right arm, but the lower extremities did not show this. The left subclavian could be felt to be large and firm but pulseless.

On March 11th her chest was examined by Dr. Smith and myself. Her right lung appeared out of commission. Both front and back were absolutely dull, except at the apex. No breath sounds were heard except at the apex. Vocal fremitus and tactile fremitus were both absent. The heart sounds were greatly exaggerated at the pulmonary area.

The condition was somewhat of a puzzle to us at this stage. Was it pneumonia? The dullness and the high temperature (still 104°) would suggest this, but the lack of any breath sounds did not fit in. It was thought that some circulatory disaster like a massive infarct or thrombosis of the pulmonary arteries was more likely.

March 12th.—Some rusty sputum appeared, and a papular rash on some parts of the trunk.

March 13th.—Dr. Gilmore took an x-ray plate with a portable machine. His report "Examination of the chest reveals complete obscuration of the lower two-thirds of the lung field on the right. The interspaces are expanded. The heart is definitely pushed to the left. Findings indicate pleural effusion with no evidence of the underlying pathology of the lung."

From the 13th to the 17th there was little change in her condition. Her temperature remained constant at 102° and pulse from 120 to 130. At this time I placed on the progress record this suggestion "It might be a retrograde embolism, a clot passing up through the pelvic veins and through a patent foramen ovale and down through the brachial artery to the juncture of the radial and ulnar, other clots passing later through the pulmonary artery to the right lung, forming massive infarct of the right lung, possibly also to the lower lobe of the left lung."

On March 17th I received a letter from Dr. Wilcox suggesting aspiration of her chest. After consultation with Dr. Smith we did so, but only were able to withdraw about a dram of dark fluid blood. This was sent to the laboratory at London for culture, but it was reported sterile.

Two days later, on the 19th, she seemed a little better in the morning, but about 11.30 a.m. she began to cough up a large quantity of greenish sputum of foul odour. Later the sputum became brownish and thin, but still foul. In all at this time she brought up about ten or twelve ounces of fluid. About 10 p.m., while Dr. Wilcox and myself were present, she became cyanosed, depressed and sweating. She was turned on her face and expectorated about 1 oz. of putrid yellow sputum, and felt better. While on her face we examined her chest. Dullness over the right chest, less marked on the left. On the right side an area about four inches in diameter could be outlined, of increased resonance; amphoric breathing and pectoriloquy. The surrounding area was dull and scattered râles were present. Left lung essentially clear. The heart was still displaced to the right. Clubbing of the fingers was developing rapidly. Evidently a large abscess had ruptured into a bronchus.

During the next two days she seemed a little better; her temperature dropped to 101°, but she had to be turned on her face several times a day to expel the sputum. It was noted that the amount of sputum decreased rapidly. Also during this time the dullness was uniform over the whole right lung, and no amphoric breathing or pectoriloquy could be detected. No evidence of any definite cavity could be made out by physical examination after the first day. This caused us to ask

for another x-ray examination which was done on March 20th. Dr. Gilmore reported "Examination reveals a high diaphragm on the right side. The heart is displaced to the left to a lesser degree than formerly. A huge cavity or limited pneumothorax is present in the right middle lung field with a smaller in the right hilum region. The right apex shows congestion. The right base shows atelectasis. The costo-phrenic angle is obscured by either a small amount of fluid or pleural thickening."

Two days later, the 22nd, she was very tired and ate very little. About nine o'clock p.m. she suddenly became very ill and expired in a few minutes.

AUTOPSY

A partial examination of the body was made 2½ hours after death, and after embalming had been done.

The body was that of a well nourished woman of about thirty years of age. The left arm was black and the skin dry as high as the elbow on the outer side and about two inches above the elbow on the inner side. The skin was discoloured on the inner side as high as the axilla, but of normal appearance on the outer side to about an inch above the elbow. The left hand was dry and shrivelled like a mummy. The dry and moist skin was sharply demarcated.

On opening the chest cavity the left pleura was found to be free except for a few bands, and only a little fluid was present (about an ounce). The left lung showed some œdema at the base, but was otherwise normal. The right lung was densely adherent except at the apex, where the fingers only could be inserted. The adhesions were so dense that the diaphragm had to be removed before the right lung could be taken out. In separating the pleural adhesions on the outer side of the chest a cavity containing air was opened. The air was under considerable tension, for it escaped with an audible sound; it had a very foul odour. This was a limited pneumothorax, limited in extent by the dense adhesions and extending between the upper and lower lobes of the lung. It was evidently the cavity that showed in the last x-ray picture. The subclavian artery was found to be very hard and was removed with the heart and aorta. It was filled with a firm clot and this clot protruded into the aorta. This protruding portion was firm and tough and worm-like in shape, extending about an inch into the aorta. It was not a post-mortem clot. The superior vena cava and subclavian veins were free from clots.

There was about an ounce of clear fluid in the pericardial cavity. The heart was normal. The valves showed no abnormality. The foramen ovale was patent, and a wormlike clot was hanging through it into each auricle. This clot was about ¾ inch into the left auricle and about ¼ inch into the right auricle. When removed the right lung was found to be normal in appearance and consistence in the upper lobe. The lower was dull in colour, airless, and apparently gangrenous. On section, no cavity of any size was found, though pus could be squeezed out of portions of it. When the diaphragm was removed it was found that the liver was very high in the thorax, reaching up to the level of the third rib.

The abdomen was not opened nor was the brain.

The origin of the clot in the brachial artery is still obscure. From its sudden onset it would appear that it was most likely an embolism rather than a thrombosis. The suggested explanation is still tenable, of a retrograde embolism, the clot originating in the pelvic veins *post partum*. The foramen ovale was patent, and the presence of a clot lying in the opening would indicate that there had been some current passing through the opening. The objection to this is that the *post-partum* clots do not separate until about the tenth day or later. This happened the second day after delivery. Another objection is that the pressure is greater in the left auricle than the right. Still, though rare, retrograde embolism does occur.

Another explanation possible is that the original clot formed in the foramen ovale itself, extending into each ventricle, from which a portion detached itself into the left auricle and from there into the auricle and the subclavian and brachial arteries. The other end of the clot may have been the origin of the clot that caused the infarct in the right lung. I am rather inclined to favour this explanation.

We had expected to find some clots in the pulmonary arteries, but none were found. Probably they were small and passed into some of the smaller branches, or they may have been absorbed. No other explanation of the lung condition than an infarct is evident. Primary thrombosis of the pulmonary artery is unknown. Three sources of the clots are possible: (*a*) from the pelvic veins; (*b*) from the gangrenous area in the arm; or (*c*) from the clot in the foramen ovale. Had a clot large enough to be found *post mortem* been caught in a branch of the pulmonary artery it would have undoubtedly have caused sudden death. An abscess had formed in the dead area of the lung which later ruptured into the pleural cavity and also into a bronchus. The opening into the bronchus closed and left the localized pneumothorax which showed in the x-ray picture. The clot in the subclavian artery must have extended up along the artery from the original clot, most likely at the bifurcation of the radial and ulnar arteries. From the tag-end extending into the aorta a fragment must have floated off and into the adjacent left carotid and into the brain, causing her sudden death.

The spreading of the clot upwards through the brachial and subclavian arteries seems to show a blood dyscrasia that caused too free clotting of the blood. I have no explanation to offer as to the nature of the abnormality of the blood. The only thing in the history previous to the embolism was the persistent vomiting during and for three days after her confinement.

A CASE OF INFESTATION WITH THE CORN BORER, *PYRAUSTA NUBILALIS*, (SCOLECIASIS)

BY H. B. CHURCH, M.D.,

Aylmer East, Que.

The following case has been judged worthy of record on account of its extreme rarity.

On August 24, 1936, I was called to see a woman who was said to have had a "fit". The patient was 58 years old, a widow. There was no evidence of any convulsions, as far as I could see, but she was evidently very uncomfortable and restless, and complained of intense itching and irritation of the vagina.

The history showed that she had had three healthy children, and no serious illnesses in the last five years. She had been quite well up until the day before, but woke at six in the morning of the day of my visit with what she described as a "queer feeling" in the vagina. This became an intense itching and soreness, with inability to urinate. She thinks she fainted, and when she recovered found that the bed was wet.

The examination showed a well nourished and well developed elderly female. The heart was clear; the lungs and abdomen were negative. The temperature and pulse were normal. The reflexes were present and normal. The vagina showed intense reddening, with a moderate whitish discharge. The urethral orifice was œdematous, but a catheter passed quite readily.

A mild vaginal douche was ordered, but there seemed to be no definite reason for her complaints. At two o'clock next morning I was again summoned, on account of the patient having another "fit". Again I could find no signs of convulsive seizure, but the patient was extremely restless and irritable, and could not stay quiet. As before, she complained of vaginal itching. Examination now showed that there were three symmetrical œdematous blebs around the orifice of the urethra, with what appeared to be a whitish mucous plug in the opening itself. On catching this plug and pulling on it, a live worm about three-quarters of an inch long was extracted. Once the plug was removed a large quantity of urine followed, which had evidently been under some pressure.

There was immediate relief and the itching and discomfort soon began to disappear. I followed the case for the next three weeks, and in that time all the symptoms entirely cleared up. Mild antiseptic treatment was followed.

The worm was identified for me by the Entomological Branch of the Department of Agriculture at Ottawa, as the European corn borer, *Pyrausta nubilalis*. In his letter to me on the subject Mr. C. R. Twinn, Assistant Entomologist, said that human infestation with this type of larva is extremely rare, and I have been unable myself to find reports of any similar case. But, considering the enormous numbers of these insects on farms in Eastern Canada, it is possible that it has occurred before.

The Entomological Department have kindly given me full details regarding this borer, which apparently is one of the most serious menaces to the corn crops in Canada and the United States. It was first discovered in Canada in 1920, and the infestation has been so severe in the counties of Essex and Kent, Ont., that in 1926 the corn crop was practically ruined over an area of about 1,200 square miles.

The borer is a caterpillar about 7/8 of an inch long. These insects eat into the corn stalks and cobs, and remain in their tunnels until their development into pupæ, and later, moths. The moths come out to lay their eggs in early summer, and as they fly only at night they are rarely seen. The eggs are found on the under sides of the corn leaves, and one female moth was found to lay as many as 1,210 eggs while under observation. The eggs practically all hatch in from three to eight days, and the young caterpillars then enter the stalks as already described.

It is a matter for some speculation as to how my patient acquired the infestation, as the larvæ cannot live in the human intestinal tract. It is possible that the insect gained access to her person either by directly crawling under her light summer clothing, or by some unclean personal habit.

I wish to express my thanks to Dr. Gibson, Dominion Entomologist, for his assistance and identification of the worm found.

DEATH FROM VAGINAL INSUFFLATION

BY S. J. S. PEIRCE

The Bigelow Clinic,

Brandon

The following case history indicates the necessity for care in selecting cases for vaginal insufflation.

A woman, aged 26, who had had one child, was under treatment for vaginal trichomoniasis. She was pregnant four months. The physician had painted the vaginal vault with mercurochrome, then ballooning up the vagina under slight pressure, had insufflated an antiseptic powder. The patient immediately declared that she felt "funny", and in a few minutes was dead.

Autopsy was done about twenty hours after death, and after the body had been embalmed, which had been done immediately after death. The body was that of a well-nourished young woman, showing no marks of external violence. The abdominal organs appeared to be normal. The uterus was enlarged consistent with four months' pregnancy. The wall was soft and flabby, and the superficial venous sinuses filled with air. Section into the uterus released a puff of air, which lay between the membranes and uterine wall. There was no sign of pelvic inflammation. On removing the uterus from the body it was

found that very slight pressure exerted on the cervical canal was sufficient to balloon up the organ with air. The membranes were intact, but not adherent to the uterine mucosa anywhere except at the placental site. The latter was in normal position on the upper posterior part of the fundus. The placenta at its upper part was separated from the uterine wall to one-tenth of its extent, but there was no blood in the uterine cavity. The vena cava and all visible blood vessels, including the coronary and cerebral vessels, contained air. None of the organs showed any definite pathological changes beyond the presence of air in the vessels.

The conclusion seemed unavoidable — that death was due to an air-embolus, the air having entered the vascular system through patulous uterine sinuses.

Treatment of vaginal trichomoniasis by insufflation is being actively advised. Its use during pregnancy seems definitely contra-indicated.

Editorial

STUDIES IN INFLUENZA

THE clarification of the nature of influenza is fraught with peculiar difficulties. In the first place—what is influenza? Is it a definite entity or is it only a fulminating form of "the common cold"? In times of epidemic diagnosis is usually easy. We have an acute illness, of brief incubation, characterized by sharp fever, catarrh of the respiratory tract, with a tendency towards involvement of the nervous system in the form of intense headache, pain in the back, and sometimes delirium, and towards pneumonia. But there are milder cases and abortive forms. Between epidemics we find sporadic cases which resemble influenza, but may not be. Here personal opinion comes into play and judgment is difficult. Competent authorities believe that "sporadic" influenza is not an entity. We cannot decide this matter now. Then, there is the question of the infective agent. At first, Pfeiffer's bacillus was thought to be the cause, on its discovery in 1892. During the Great War, however, many cases of influenza occurred in which this organism was not obtained. On the contrary, it was found in the respiratory passages of healthy people who had not had influenza so far as was known. The serological evidence, too, was not convincing. While some evidence has been adduced which points the other way, it is safe to say that at present *Hæmophilus influenzæ*, as it is now called, if a causative factor at all, is regarded as not the only one. It may, however, be associated with a virus, either alone or in association with other microorganisms. Olitzky and Gates have suggested that a filter-passer, *Bact. pneumosintes*, is the probable cause of influenza. During the Great War Sir John Rose Bradford and his associates had suggested that a filter-passer was at work. Then, it is now known that swine influenza and canine distemper have some relation to human influenza. But what is "swine influenza"? These considerations, and others might be mentioned, illustrate the complexity of the problem.

A great step forward was taken when Smith, Andrewes and Laidlaw announced that they had isolated a virus from certain cases of human influenza,[1] and then it was found that this virus was pathogenic for ferrets and could, with certain precautions, be made infective for mice.[2] These discoveries at once made it possible to study influenza on a more adequate basis. The investigator no longer had to bide his time until an epidemic came to the fore. It was now possible to maintain a strain of the infective organism for a prolonged period and study the reactive processes which it set up in the body. In short, modern methods could be brought to bear on this most elusive disease. Now, at last, we know much more about the nature of influenza, even if many points still remain to be cleared up.

By 1935 Andrewes, Laidlaw and Smith[3]

1. SMITH, W., ANDREWES, C. H. and LAIDLAW, P. P.: A virus obtained from influenza patients, *The Lancet*, 1933, **2**: 66.
2. ANDREWES, C. H., LAIDLAW, P. P. and SMITH, W.: The susceptibility of mice to the viruses of human and swine influenza, *The Lancet*, 1934, **2**: 859.
3. ANDREWES, C. H., LAIDLAW, P. P. and SMITH, W.: Influenza: observations on the recovery of virus from man and on the antibody content of human sera, *Brit. J. Exper. Path.*, 1935, **16**: 566.

had recovered a virus pathogenic for ferrets in 14 cases of influenza (5 in 1933; 1 in 1934; and 8 in 1935), and, in 1934, found that after several passages through ferrets it could induce infection in mice.[4] They did not find a virus in cases of "common cold" or sporadic influenza. Andrewes also noticed[4] that the virus of human and that of swine influenza produce identical phenomena in ferrets and mice, but show some differences, immunologically. To produce swine influenza in pigs the combined action of the virus and a bacillus (*Hæmophilus influenzæ suis*) is necessary, but the virus alone can produce the complete picture of the disease in ferrets and mice.

Smith[5] found that it was impossible to cultivate the virus on media free from living cells, but succeeded when he used the chorio-allantoic membrane of developing hens' eggs in a medium of minced chicken embryo and Tyrode's solution. This finding suggests a family relationship between the virus of influenza and other better known viruses, and also that a culture virus has been obtained which may possess antigenic properties and aid in the production of active immunity against influenza.

Having isolated a virus from cases of influenza, both human and porcine, the next step was to study its reactions in the body.

Numerous investigators have found that after the inoculation of the viruses of human and swine influenza antibodies are produced in the experimental animal with a certain amount of immunity which tends to be transient, in the latter particular resembling the natural immunity found in the human subject. Smith, Andrewes and Laidlaw[6] found that after recovery from infection with influenza ferrets are completely resistant to reinfection for at least three months, after which time the immunity slowly wanes. The waning immunity can be reinforced by subcutaneous inoculation of living virus, so that once more the ferret becomes completely resistant. Rather curiously, ferrets with waning immunity, but which still have significant amounts of virus-neutralizing antibodies, can be reinfected by way of the nasal mucosa. This phenomenon is still being investigated.

Francis and Shope,[7] on the basis of their experimental findings, suggest that there is some antigenic relationship, though not amounting to identity, between the virus of human influenza and that of the porcine form. Shope also,[8] advances the view, though by no means for the first time, that the organism of swine influenza is "the surviving prototype" of that responsible for the human pandemic of 1918. And Eichorn and Pyle[9] found that the inoculation of the virus of human influenza into ferrets produced immunity against canine distemper. All this reminds us of the somewhat similar problem that confronts us in connection with brucellosis.

Some other peculiar facts have come to the fore. Francis and Magill[10] have found that neutralizing antibodies for the virus of influenza are demonstrable in a large proportion of human sera. The puzzling thing about their results is that although the age-period 30 to 39 furnishes the biggest percentage of sera containing antibody the period at which the antibody is present in sufficient amount to afford complete protection is from 1 to 5 years. And, again, Dochez and his collaborators[11] have found that more often than not inoculation of human beings with the virus of influenza produced only a "common cold". No doubt continued investigation will clear up some of these difficulties. A.G.N.

4. ANDREWES, C. H.: Influenza in man and animals, *Brit. M. J.*, 1935, **1**: 495.

5. SMITH, W.: Cultivation of the virus of influenza, *Brit. J. Exper. Path.*, 1935, **16**: 508.

6. SMITH, W., ANDREWES, C. H. and LAIDLAW, P. P.: Influenza: experiments on the immunization of ferrests and mice, *Brit. J. Exper. Path.*, 1935, **16**: 291.

7. FRANCIS, T., Jr. and SHOPE, R. E.: Neutralization tests with sera of convalescent or immunized animals and the viruses of swine and human influenza, *J. Exper. Med.*, 1936, **63**: 645.

8. SHOPE, R. E.: The incidence of neutralizing antibodies for swine influenza virus in the sera of human beings of different ages, *J. Exper. Med.*, 1936, **63**: 669.

9. EICHORN, A. and PYLE, N. J.: Observations on relationship of virus of human influenza and dog distemper, *J. Am. M. Ass.*, 1934, **102**: 2082.

10. FRANCIS, T., Jr. and MAGILL, T. P.: Incidence of neutralizing antibodies for human influenza virus in serum of human individuals of different ages, *J. Exper. Med.*, 1936, **63**: 655.

11. DOCHEZ, A. R., MILLS, K. C. and KNEELAND, Y., Jr.: Studies on the virus of influenza, *J. Exper. Med.*, 1936, **63**: 581.

THE MORTALITY FROM THE PRINCIPAL CARDIO-VASCULAR-RENAL DISEASES

THE statistical bulletins published from time to time by the Metropolitan Life Insurance Company are always illuminating and deserving of careful study. They call attention to important trends in the march of disease as it affects mass populations, and frequently indicate lines of endeavour which could be profitably followed up by the medical profession. The latest production of this kind which we have seen is Monograph No. 4 and this is no exception to the general rule. It is entitled "The Mortality from the Principal Cardio-Vascular-Renal Diseases" and is a study of heart disease, chronic nephritis, arterial disease, angina pectoris, and cerebral hæmorrhage as exemplified in the industrial policy-holders of the Company during a twenty-year period, from 1911 to 1930. While the group of diseases embraced under the general heading "Cardio-vascular-renal" and their interrelations have been fully recognized by the medical profession for years it is rather curious that the question of the mortality from these diseases has, statistically-speaking, been scarcely explored. Dr. L. I. Dublin, the statistician of the Company, thinks that the attitude of fatalism which has been and still is a concomitant of the subject has been inimical to research. Monograph No. 4 seems to offer hope of better things.

The statistical study of cardio-vascular-renal disease presents special difficulties. We all know that the component entities which are grouped under the term "cardio-vascular-renal" are closely interlocked. It is difficult, often impossible, to state which one is the primary. The attending physician in any given case is apt to give the most obtrusive or, perhaps, the last, clinical feature as the cause of death; it may not be. In any event he is not always in a position to appraise the relative value of the possible etiological factors. Then, during the period under review the quality of medical practice has changed rapidly and there have been shifting standards for the recording of mortality statistics. Statistics of the kind that we are discussing are therefore open to criticism. By considering the various conditions as a whole most of the objections that can be raised, however, lose much of their weight. In any event, the analysis made by the Metropolitan Life Insurance Company affords a *point d'appui* for a more exact study of the question as conditions, which are admittedly unsatisfactory, improve.

During the past forty or fifty years the centre of gravity, so to speak, has shifted. With the perfecting of public health measures and the discovery of vaccines and protective sera we have obtained very considerable control of the infectious group of diseases, a control which in many cases would be absolute could we obtain more whole-hearted support from the general public and their representatives. The result of this is that more persons are being spared in childhood and youth to reach the period of middle and old age, when the wear and tear of life, the degenerative processes, and cancer, take their toll. Infectious diseases bulk less large as causes of death, while cardio-vascular-renal diseases and cancer easily top the list. It is stated that in the United States fifty out of every one hundred children born will die from one or other of the cardio-vascular-renal diseases. This is five times the number of deaths to be expected from cancer, and ten times that from tuberculosis. We come now to a more detailed analysis of the monograph.

In the twenty-year period under review the principal cardio-vascular-renal diseases accounted for more than 25 per cent of the deaths from all causes. The relative importance of these conditions has increased as time went on. Whereas during 1911 to 1915 they comprised 26.8 per cent of the deaths from all causes, from 1926 to 1930 the figure had risen to 32.1. The mortality increases with advancing age, with the largest increments at the older ages. At the ages of 25 to 34 cardio-vascular-renal diseases accounted for slightly more than 10 per cent of all deaths, and from 65 to 74 for approximately 55 per cent. In the aggregate, males had a higher death rate than had females, and the coloured race than the white.

Taking the individual components of the group, heart disease is by far the most important item, accounting for 54.3 per cent of the death from these conditions. It is interesting to note that in the second decade of the period studied chronic valvular disease and chronic myocardial disease showed opposite trends. The former showed a downward trend, while the latter manifested a sharp upward movement. Possibly, this situation reflects the better control we have of rheumatic fever, pneumonia, and many of the infections. We do not know.

Chronic nephritis is second in importance among the cardio-vascular-renal diseases, being responsible for 27 per cent of the deaths. Cerebral hæmorrhage accounted for 21.5 per cent; disease of the arteries for 4 per cent, and angina pectoris for 2.2 per cent of the deaths.

The great majority of the deaths attributed to arterial disease are certified as due to arteriosclerosis. For the period 1922 to 1930 the mortality from this condition was fairly stable. The number of deaths from arteriosclerosis affords no index of the extent to which arteriosclerotic processes are responsible for the mortality from cardio-vascular-renal conditions. Most deaths which are the end-result of arteriosclerosis are allocated to heart disease, chronic nephritis, or cerebral hæmorrhage.

The death rate from the group of diseases under consideration is higher in the urban centres and highest among unskilled workers. Professional men come next in regard to vulnerability. While the trend of mortality from cardio-vascular-renal diseases in the industrial policy-holders of the Company follows the same curve as in the case of the general population the level of the death rate is higher in the former.

The monograph points out, very rightly, that cardio-vascular-renal diseases fall into two main classes—those that are due to earlier infections, such as rheumatic fever, syphilis, typhoid fever, and the communicable diseases of childhood, and those that reflect rather the breakdown of the organism due to internal mal-adjustment or to senescence. There is perhaps not much to be done for the second class, at least, at the moment, but much more could be done for the first than is being done. We commend this matter to medical men. Knowing what we do in regard to possible sequelæ in the case of the various infections it surely is justifiable to insist on the necessity of following up these cases until we are satisfied that there are no sequelæ, or, if there are, that an attempt is being made to control them. Most of us realize the dangerous consequences that are possible in the case of rheumatic fever and syphilis, and act accordingly, but are we sufficiently alive to the danger from, say, a dilated heart in typhoid fever, or from nephritis in scarlatina? It is not sufficient to see the patient safely through the attack and then dismiss the matter from the mind. This is a good place, also, to insist on the value of the periodic health examination. Care along these lines would soon make an impression for the better in the case of cardio-vascular-renal disease.

A.G.N.

Editorial Comments

The Management of the New-born Baby*

This useful little brochure, of less than fifty pages, is intended as a guide for mid-wives. The author, Dr. Alan Moncrieff, who is our London correspondent, is well known as a pædiatrician and brings a wealth of experience to his task. He states in his introduction that remarkable strides have been made during this century in reducing the infant mortality rate to about half what it was in the closing years of the eighteen-hundreds, and in each thousand live births fifty to sixty babies now survive the first year who would die were it not for the great improvements effected mainly by the Infant Welfare movement. He notes, however, the unfortunate fact that the number of deaths occurring during the first month has not decreased to anything like the same extent. This first month is the period during which the mid-wife, rather than the mother, is responsible for the infant's welfare, and so his little book is intended to interpret for the practising mid-wife the latest methods for securing the health of the new-born baby. It is

* The Management of the New-born Baby: a Guide for Mid-wives. Alan Moncrieff, M.D., F.R.C.P. Price, ninepence. Association of Maternity and Child Welfare Centres, 117 Piccadilly, London, W.1.

worthy of note that the methods he advises are for the most part as easily applicable in a cottage as in a well-equipped institution.

The book is logically planned. It begins with certain considerations relating to events before birth and then passes on to the normal and abnormal events that concern the early days, more or less in the order that they arise. Conditions arising before birth which should forewarn and forearm the mid-wife so that she can meet adequately the ordinary and extraordinary situations that arise subsequently are briefly outlined. Then, such matters as establishing the breathing, the general hygiene of the mother and child, lactation, feeding, artificial feeding, disorders in the new-born baby, congenital malformations, and the management of prematurity are simply and lucidly set forth. When a physician's services should be requisitioned in particular emergencies is carefully pointed out.

Dr. Moncrieff is Physician to the Children's Department. Middlesex Hospital; Physician to Out-Patients, Hospital for Sick Children; Assistant Pædiatrician, Queen Charlotte's Maternity Hospital, and Consulting Pædiatrician, British Post-Graduate Medical School. He can therefore be read with confidence. In Canada we do not have the mid-wife system to anything like the extent that it prevails in Europe. In the cities and towns the trained nurse plays the rôle — in the remote country places, the "handy woman". We feel, nevertheless, that Dr. Moncrieff's little book, divested of technical expressions as it is, and small enough to be carried with the working kit, would be of valuable assistance to all those having the care of the new-born baby, not even excluding the mother (nor perhaps, the father!). The subjects are dealt with in such a simple, clear and straight-forward manner that the book is altogether admirable. It is ninepence (plus postage) well invested.

A.G.N.

Noise in Montreal

At long last something is being done to lessen the amount of noise in Montreal. Not any too soon. A certain amount of noise is unavoidable and we must put up with it if we desire to enjoy the advantages of living in a city. Yet all will agree that we have a surfeit of it, largely because of carelessness, thoughtlessness, or downright selfishness. Professor H. E. Reilley, of the Department of Physics of McGill University, and Chairman of the Montreal Noise Abatement Committee, is leading the fight, and has been conducting experiments in various parts of the city, in order to find the noisiest areas and to classify the different sorts of noises. Fortunately, an old by-law which imposes a fine of $40 on noise makers has been resurrected from oblivion. It empowers the police to deal with offenders in the matter of unnecessary noise production, and, we understand, the authorities have promised to put its provisions into effect. The Board of Health is also actively cooperating in the good work. Those of us who live in apartment houses, who are disturbed at 3 a.m. by the breaking-up of convivial parties, with the starting of numerous motor cars, at 4 a.m. by the passing of the jaunty milk cart, and at almost any time by the asinine person who is too lazy to get out of his car to summon his girl, but prefers to annoy perhaps fifty families by honking his horn, will rise up and call Professor Reilley blessed if he succeeds in his endeavour. We intend to return to this most important subject, when we shall deal with it more at length. By all means let the crusade go on.

A.G.N.

Narcotics

The Report of the Narcotic Division of the Department of Pensions and National Health for the year ending March 31, 1936, has just come to hand. This is an excellent report which might be read with interest by every physician in Canada. Of particular interest to the medical profession are the following extracts which we have taken the liberty of quoting from the report:—

"The cooperation with the medical profession has continued to be very close, and we are greatly indebted to many members thereof for their assistance and cooperation in relation to cases of addiction which, not having underworld associations, offered reasonable prospects of cure. The facilities of the Ontario Hospitals, rendered available by recent provincial legislation, have been utilized to a considerable extent in that connection, and have aided materially in the constructive work which is possible along that line."

"There are now two provinces, Manitoba and British Columbia, in which amendments to the provincial Pharmacy Acts have ensured that straight codeine shall only be sold by retail druggists on medical prescription. This is a most useful provision."

"During the year it became necessary to prosecute two physicians. One case, involving circumstances which clearly indicated illicit intent, resulted in a sentence of four years' imprisonment, while the other, in connection with which narcotics were sold to a perfectly healthy person on a number of occasions, resulted in a fine of $200 or three months' imprisonment."

While it is regretted that the authorities found it necessary to take action against two physicians, it is a matter of congratulation to the profession in that two out of a medical population of approximately 11,000 indicates a splendid record for the profession as a whole.

A.G.N.

Special Articles

THE RED MAN AND THE WHITE PLAGUE*

BY DAVID A. STEWART, M.D., LL.D.

Medical Superintendent, Sanatorium Board of Manitoba

Ninette, Manitoba

We can all remember when tuberculosis among Indians was thought of as a kind of relentless process of nature, like an earthquake that we could stand in awe of, and be very sad about but do nothing to check or change. Now we know, or if we don't we should, that tuberculosis among Indians is amenable to suitable and adequate measures of prevention and cure, just as it is among white people, and just as any other endemic and epidemic disease is in any population. This field once thought to be abandoned to stark fate could yield returns to surprise everybody.

Much has already been done by the Federal government through its Department of Indian Affairs to improve standards of living, health and enjoyment of life among its native wards, but very much more remains to be done by direct attack on entrenched disease, chiefly tuberculosis. An excellent illustration is the cutting of death rates in two, in five years, in the Health Demonstration carried on by the Department at Fort Qu'Appelle as a result of full-time medical care, some segregation, and a limited amount of hospitalization. Still better results will follow—perhaps another cut in two of death rates—when this unit has the backing also of a small local hospital which has just been completed by the Department. There is no reasonable doubt that Indian deaths and Indian tuberculosis can be reduced in time to an astonishing minimum if only the necessary measures can be applied.

It is true that all possible helpful measures, economic, medical and educational, cannot be fully applied in every part of the field at once, especially at a time of maximal national outlay and minimal income. But we, the people of Canada, who are the guardians of the Indians, should at least know that tuberculosis and other diseases among them are not the hopeless or insoluble problems they were once thought to be. The chief obstacle is lack of money, which, while it may be at times the root of much evil, can also be a means of rooting out much evil. One way to lessen that obstacle, if we cannot overcome it, is to find the most efficient ways of using what money and resources are already devoted to the service of Indians. For instance, the local medical services, while here and there worthy of all praise, could be greatly improved, especially if made when possible full-time, reasonably continuous, and specially trained. The axe should hew straight to the line of the utmost that can be done for the health and well-being of the Indians, letting political and other chips fall where they will.

Not only do we owe the Indian this fair treatment because we took and occupied his country, but especially because we brought him the disease, tuberculosis, and so should help him to fight it. Furthermore, inter-communications of all kinds between Indians and white people, on account of new means of transportation and in the opening up of the North, are steadily increasing, and ought to be. These Indian reservations and settlements never were water-tight or disease-tight compartments, and in a new day of easier travel are becoming less and less so. And it is true that any disease in any remote corner of a province is *disease of the province;* that the province will not be clear of any disease nor safe from its menace until every group is clear and safe; and that in health matters no man liveth unto himself and no man dieth unto himself.

Treaty Indians are not citizens, but they are residents within the provinces just as though they were citizens; so their uncontrolled diseases are a menace to citizens generally and to the collective general health of the provinces, just as though they were citizens. Indeed their menace is in some ways much greater when they are not citizens, because they are outside of all local and provincial agencies, arrangements and facilities. A reserve with bad conditions is as a city slum would be if exempt from city health authorities and regulations. The Indian as a dangerous neighbour, though a problem in the eastern provinces, is a much greater problem in Ontario west of the Great Lakes, the four western provinces, and, to a lesser degree, in the northern hinterland. The problem is less there because primitive Indian life has been less interfered with. As given by Ottawa, that is, with occasionally a few added outside of reserves, especially in recorded deaths, Indians, in all Canada represent 1.1 per cent of the population; in Prince Edward Island, 0.3 per cent; in Nova Scotia, New Brunswick and Quebec, 0.4 per cent; in Ontario, 0.9 per cent; in Manitoba, 2.2 per cent; in Saskatchewan, 1.7; Alberta, 2.1; and in British Columbia, 3.5 per cent.

It may be thought on first glance that such a small proportion of Indians could not greatly affect the general average of health or the general tuberculosis death-rate; but this is how the records stand in the four western provinces in 1934. In Manitoba the Indians are only

* A paper read last June at the Annual Meeting of the Canadian Tuberculosis Association in Vancouver.

2.2 per cent of the population, yet 31 per cent of all deaths from tuberculosis were among this 2.2 per cent. In Saskatchewan 27 per cent of the total tuberculosis deaths fell among the Indians, who are only 1.6 per cent of the population. In Alberta 2.1 per cent Indians accounted for 34 per cent of the tuberculosis deaths, and in British Columbia an Indian population of 3.7 per cent suffered 35 per cent of the deaths from tuberculosis.

From these reservoirs of tuberculosis, how does infection leak into the ordinary community? By three ways; first, mixture of blood, which has gone on for nearly two hundred years, and will no doubt continue until the red race is absorbed into the general population. This forecast surely gives a special motive for doing the best we can for the Indians who are actually increasing in numbers in spite of all their difficulties. Secondly, disease is scattered by the association of Indian people with whites in work, travel and exploration. And thirdly, it can be spread by articles of Indian make or Indian handling. Even the blue-berry picking and selling might be considered in this connection. The menace of these slum areas among us becomes greater and greater as the better communities clean up. Now, when some local areas are practically clear of tuberculosis infection, and children are growing up uninfected and tuberculin-negative, any stray outside infection is a spark in dry grass, not a spark in the rather sodden grass of a half or even a quarter of a century ago.

We have been accustomed to think of the Indian's lack of resistance to tuberculosis as entirely racial. It is, of course, partly due to this white man's disease being a new one, and, like a new broom, sweeping clean. We have in mind the old rule that all newly introduced infections are especially virulent, and all specially virulent infections are newly introduced. In that it is a comparatively new disease the Indian has handicap enough. And the bad conditions and carelessness of the Indians in the matter of infection and its spread make infection and reinfection a matter of daily possibility and probability. But there is no doubt that a great part of the Indian's low resistance to tuberculosis is due to his abject poverty. Like most other social problems this one is less medical than economic and educational. It is true, of course, that this poverty is accentuated by his own mismanagement, indolence, and improvidence, and that these are sometimes gross. However, we must remember that the Indian is in the difficult position of having almost lost his own world of the open spaces and their various employments, while he has only small and occasional chances in the white man's world. The most energetic and resourceful white man, if put where some Indians are, and under their limitations in employment chances, would likely not do much better than the Indians have done. Race, carelessness, and ignorance handicap the Indian in his fight—if he does fight—against tuberculosis, but his poverty also presents great difficulties.

We are the guardians of the Indians, we, the people of Canada. In the language of the day, we have a mandate for their care. The world suffers increasing spasms of conscience about what is done by dominant peoples like ourselves with native races such as the Indians. The new principle, that the advantage of the native in and through his own country and not the enrichment of the invader from the native's toil or slavery, is the first aim of any kind of colonization would have been preposterous to Cortes and to most of his successors. In Canada we have likely done neither the worst nor the best possible, but I doubt if a League of Nations mandate committee would be entirely satisfied with what we have done or are doing for the health of our wards or the lessening of tuberculosis among them. At any rate something more could, should, and, in the long run, must be done, for the Indians' own sake, and to remove from the doorsteps of ordinary communities this anomaly of nuisance and menace which they suffer from but cannot locally control.

The Canadian Tuberculosis Association, in session at Vancouver in June, 1936, resolved to bring respectfully to the attention of the Government of Canada certain facts about the Indians of Canada, and to submit certain recommendations based on these facts:—

SOME FACTS

1. The general death rate among Indians is extremely high, especially in deaths from diseases of the chest.

2. Tuberculosis in the western provinces has a death rate among Indians ten to twenty times as great as that among white people, and over 30 per cent of the total deaths from tuberculosis occur among the Indians, who comprise less than three per cent of the total population.

3. Where well-thought-out measures have been applied by the Department of Indian Affairs the response of the Indians and the comparative clearing-up of their disease have been phenomenal.

4. We are satisfied that this extremely high death rate can be reduced, as death rates elsewhere have been reduced in time, by the careful applying of known measures.

5. Such tuberculosis-soaked groups as the Indians, mingling with the general population in the western provinces, constitute a very great menace to the health and life of the people in general.

6. The rapid lessening of tuberculosis in the general populations of the western provinces, while this disease remains among the Indians unabated, makes the relative danger of the spread of infection from Indians a constantly increasing one.

7. Whatever the menace may be, and however

well understood by people of the provinces, no action can be taken except by the federal authorities.

RECOMMENDATIONS

1. In view of the above facts, we submit that, wherever possible, the medical services given to the Indians should be full-time, permanent appointments.
2. Medical services among the Indians should be considered to demand special experience and skill in dealing with diseases of the chest, especially tuberculosis, and such experience and skill should be chief considerations in the making of appointments.
3. The services of travelling clinics with x-ray equipment, either organized by the Department or borrowed from provincial organizations, can and should be used for periodical surveys of reserves.
4. Such surveys should be made at least yearly in schools for Indian children, and children who have infective disease should be satisfactorily segregated or removed.

Men and Books

MEDICINE AND POETRY

BEING AN ACCOUNT OF THOSE SONS OF ÆSCULAPIUS WHO HAVE ON OCCASION PAID HOMAGE TO THE ELDER GOD, APOLLO.

"A physician should be a kind of poet."

BY E. P. SCARLETT, M.B.

Calgary

PART I.

At first glance, at least to modern eyes, any attempt to relate poetry and medicine appears to be almost an absurdity, a straining of the laudable practice of comparison beyond rational limits. It is not unlike linking the subtle flights of metaphysics and the harsh realities of cold mutton, so far has specialization destroyed our perspective in the modern world. But a little speculation reveals a different story. These two activities of the human spirit are closely linked historically, and in tradition they emerged from the same shrine in the temple of the gods. Apollo, the god of poetry, was the father of Æsculapius, the divinity of the healing art, and in Greek times those practising medicine were dignified as "the children of Apollo". The figure of Apollo, the supreme god of medicine, together with the Muses and the serene goddess Pallas Athene, the immortal exemplar of Reason and Discipline, are the ancient personifications of the great intellectual virtues which have raised us from the barbaric state. Science and poetry thus truly dwell together, and in any rounded philosophy of life they find full and mutual expression.

Both poetry and medicine go back to the childhood of the race. For while "poetry, like Beatrice, was born under a dancing star," medicine came into being with the first struggles for existence under the noonday sun, and under the fear of the terror that walketh by night. They have been man's spiritual companions all down the long journey. This kinship between poetry and science has been expressed by many writers. Poetry, says Bacon, "doth raise and erect the mind, by submitting the shows of things to the desires of the mind; whereas reason doth buckle and bow the mind unto the nature of things." Wordsworth in his preface to *Lyrical Ballads* describes the relation even more adequately—"Poetry is the breath and finer spirit of all knowledge; it is the impassioned expression which is in the countenance of all Science." The business of science is to accurately observe and describe— "To express what then I saw"; this done, poetry's function is to

> "add the gleam,
> The light that never was, on sea or land,
> The consecration, and the Poet's dream."

To revert to our title and set it forth in more accurate fashion, while physic requires no definition, poetry, like many of the best things in life, defies definition. The only way to know what poetry is is to read it. The appreciation of poetry has been bedevilled by the too generally accepted idea, brewed in some witch's cauldron of folly, that poetry is a rather pallid cult of abnormal or weirdly intellectual persons. The truth of the matter is that poetry is natural to man. This fact may be abundantly proved by watching any group of men who are not necessarily under the spiritual instancy of alcoholic nectars lustily roar some current song or ballad with emotional fervor and a far-off expression in their eyes. And, if poetry eludes definition, it may be set forth by example in a thousand ways. For instance, modern science proclaims that, in the scale of the universe as we know it, man is a mere speck, an impotent creature. But only poetry can state this fact adequately.

> "One generation passeth away, and another generation cometh: but the earth abideth forever — Then I looked on all the works that my hands had wrought, and on the labour that I had laboured to do: and behold, all was vanity and vexation of spirit, and there was no profit under the sun."—Ecclesiastes I: 1-11.

Or again,

> "Tomorrow, and tomorrow, and tomorrow,
> Creeps in this petty pace from day to day,
> To the last syllable of recorded time,

And all our yesterdays have lighted fools
The way to dusty death. Out, out, brief candle!
Life's but a walking shadow, a poor player
That struts and frets his hour upon the stage
And then is heard no more: it is a tale
Told by an idiot, full of sound and fury
Signifying nothing."—Macbeth V, 5.

Definition or no definition, that is poetry!

The relation of science and poetry recalls two notable passages which incidentally set forth the nature and function of poetry. The first is from the *Defence of Poesy* by Sir Philip Sidney.

"Now, therein, of all sciences (I speak still of human, and according to the human conceit) is our poet the monarch. For he doth not only show the way, but giveth so sweet a prospect unto the way as will entice any man to enter into it . . . . He beginneth not with obscure definitions, which must blur the margin with interpretations and load the mind with doubtfulness; but he cometh to you with words set in delightful proportion, either accompanied with, or prepared for, the well-enchanting skill of music; and with a tale, forsooth, he cometh unto you—with a tale which holdeth children from play and old men from the chimney corner: and, pretending no more, doth intend the winning of the mind from wickedness to virtue, even as a child is often brought to take most wholesome things by hiding them in such other as have a pleasant taste, which, if one should begin to tell them the nature of the aloes or rhubarbum they should receive, would sooner take their physic at their ears than their mouth. So it is in men —most of whom are childish in the best things till they be cradled in their graves."

The other passage is from an essay written by Matthew Arnold fifty-four years ago.

"More and more mankind will discover that we have to turn to poetry to interpret life for us, to console us, to sustain us. Without poetry, our science will appear incomplete; and most of which now passes for religion and philosophy will be replaced by poetry. Science, I say, will be incomplete without it . . . . Wordsworth finely calls poetry the breath and finer spirit of all knowledge . . . . The day will come when we shall wonder at ourselves for having trusted to them," (current philosophy and religion) "for having taken them seriously, and the more we perceive their hollowness, the more we shall prize *the breath and finer spirit of knowledge* offered to us by poetry."

But, you say, this is all very well, but to a man whose ear is tuned to the exact phrases of science poetry means nothing. He can find no satisfaction in reading poetry; his fate is not unlike that of Darwin who after years of science lost his appreciation of music. The answer to such a plaint is—"why did you ever give up reading poetry? You used to enjoy it."—

"London Bridge is broken down,
Dance o'er my Lady Lee,
London Bridge is broken down
With a gay lady."

For, as Lynd says, every child is a poet from the age at which he learns to beat a silver spoon on the table in numbers. And later at every great hour of his life—hours of love or sorrow—his deeper emotions find no expression in common speech and at such times he must be inarticulate or find speech in poetry.

For, indeed, poetry is infinite in its variety. It may proceed from the lowest to the highest. Let us try to set out such a gradation.

"Tom he was a piper's son,
He learned to play when he was young,
But all the tunes that he could play
Was, *Over the hills and far away.*"

Childish, you say; but the last line is the stuff of pure poetry. Poetry, too, depends not only on verbal music but also on the association of the words employed. Sir John Squire, a modern master of parody, illustrates this by devising a set of lines in which the names of diseases conjure up music if we could forget their association. Thus:—

"So forth then rode Sir Erysipelas
From good Lord Goitre's castle, with the steed
Loose on the rein; and as he rode he mused
On knights and ladies dead; Sir Scrofula,
Sciatica, he of Glanders, and his friend
Stout Sir Colitis out of Aquitaine,
And Impetigo, proudest of them all,
Who lived and died for blind Queen Cholera's sake . . .
And then once more the incredible dream came back,
How long ago upon the fabulous shores
Of far Lumbago, all of a summer's day,
He and the maid Neuralgia, they twain,
Lay in a flower-crowned mead, and garlands wove,
Of gout and yellow hydrocephaly . . . .
Cirrhosis and that wan, faint flower
The shepherds call dyspepsia. Gone, all gone:
There came a night he cried, 'Neuralgia!'
And never a voice to answer. Only rang
O'er cliff and battlement and desolate mere
'Neuralgia!' in the echoes' mockery."

A higher example still, its appeal depending on alliteration, is Coleridge's verse in *The Ancient Mariner*:—

"The fair breeze blew, the white foam flew,
The furrow followed free;
We were the first that ever burst
Into that silent sea."

Proceeding, here is a stanza sounding the sad wisdom of life which has long satisfied the average man—a stanza from Gray's *Elegy*:—

"The boast of heraldry, the pomp of power,
And all that beauty, all that wealth e'er gave,
Awaits alike th' inevitable hour:—
The paths of glory lead but to the grave."

And so by degrees we come to poetry in its highest expression, sounding a requiem on man and all his works,—Prospero's last speech from *The Tempest*:—

"And like the baseless fabric of this vision,
The cloud-capped towers, the gorgeous palaces,
The solemn temples, the great globe itself,
Yea, all which it inherit, shall dissolve
And like an unsubstantial pageant faded
Leave not a wrack behind. We are such stuff
As dreams are made on, and our little life
Is rounded with a sleep."

There is no occasion to pursue the thought further. It is worth remembering, however, that one of the reasons why the Bible is cherished by man is for the poetry which it contains—its thoughts are expressed in memorable verse.

"Or ever the silver cord be loosed, or the golden bowl be broken, or the pitcher be broken at the fountain, or the wheel broken at the cistern. Then shall the dust return to the earth as it was: and the spirit shall return unto God who gave it."—Ecclesiastes, XII: 6-7.

"Set me as a seal upon thine heart, as a seal upon thine arm: for love is strong as death, jealousy is cruel as the grave: the coals thereof are coals of fire, which hath a most vehement flame."

—Song of Solomon, VIII: 6.

"Where wast thou when I laid the foundations of the earth? Declare, if thou hast understanding. Who hath laid the measures thereof, if thou knowest? or who hath stretched the line upon it? Whereupon are the foundations thereof fastened? or who hath laid the corner stone thereof; when the morning stars sang together, and all the sons of God shouted for joy?"

—Job, XXXVIII: 4-7.

Without indulging in any ethereal generalizations, enough, I think, has been said to suggest what we mean by poetry. We are concerned just now with the relation between the writing of poetry and the practice of physic, not of course in any philosophical sense. It has indeed been said that "a physician should be a kind of poet", on which aphorism Sir Clifford Allbutt remarked: "A hard saying, but to their patients what are the most scientific physicians if they know all things save the human heart?" Our task is rather to consider those physicians who have written poetry, not the mere talented dabblers in verse of whom there have probably been thousands, but those men who have achieved a measure of distinction in poetry, the most difficult of all the arts. It has been claimed by Mitchell Banks that medicine stands foremost among the professions in the number of distinguished literary men who began life in its ranks. In Renaissance times and during the following century the relation between literature and medicine was close. Those were the days of the scholar — physicians such as Linacre — and medicine was in a very special sense one of the learned professions. With the advance of specialization of knowledge, however, the connection has become less intimate, and today medicine suffers because of this fact.

When we come to review the contributions of medical men to poetry we find that there are few who have distinguished themselves in both fields. The talents required to do first-rate work in medicine are widely divergent from those essential in the writing of great poetry. Only a genius of the most varied and universal character, such as Goethe, can be preeminent in poetry and science. And, besides, divided allegiance is not infrequently fatal to personal or popular success. Physicians, therefore, who have written poetry have treated it as an oblique pursuit or have practised little medicine. Some have qualified as doctors and then abandoned the profession for some other pursuit. The list, however, is an interesting one. In 1916 Dr. C. L. Dana, in a treatise entitled *Poetry and the Doctors,* compiled a catalogue of poems written by doctors, comprising the names of 162 medical men. In 1925 Sir Humphry Rolleston, in an address on *Poetry and Physic,* mentioned over eighty medical men or medical students who had written notable poetry. And in the *Bibliotheca Osleriana* there are ninety medical men represented by their poetry, two-thirds of whom wrote prior to 1801. We purpose considering some of these names, arbitrarily following a chronological order.

The identity of sympathy existing between medical men and literature has its roots far back in the early centuries of the mediæval period, when students of medicine wandered through the medical schools of Europe under the spell of the great humanist tradition of letters. The "Gaudeamus igitur" still sung in universities is a remote echo of the eleventh and twelfth centuries when the medical students were part of the great band of scholars who roared Latin songs, drank uproariously, wenched, diced, and wrote and recited Latin lyrics. A figure who is the symbol of these times is the Archpoet who died about 1165 and who has been so brilliantly re-created in our time by Miss Helen Waddell. As she says—"He travelled light, even to immortality". A "rather disreputable figure, keen as a razor and lean as a hawk", he wanders over Europe with his patron's cloak "hugged about his tatters". After some scandal about a wench, his friends, thinking to make him respectable, pack him off to Salerno to study medicine where he remains for a time. Then he returns, burnt up with the fever of consumption, and at Pavia writes his poem, the *Confessio,* the eternal challenge against the denying of the flesh, the cry of youth in all ages, whether medical students or vagrant scholars. The poem is the greatest drinking song in the world. The Latin lines pound out their rhythm vehemently.

"Estuans intrinsecus
Ira vehementi . . . ."

"Seething over inwardly
With fierce indignation,
In my bitterness of soul,
Hear my declaration.
I am of one element,
Levity my matter,
Like enough a withered leaf
For the winds to scatter.

Yet a second charge they bring:
I'm forever gaming.
Yea, the dice hath many a time
Stripped me to my shaming.
What an if the body's cold,
If the mind is burning.
On the anvil hammering,
Rhymes and verses turning.

Look again upon your list.
Is the tavern on it?
Yea, and never have I scorned,
Never shall I scorn it,
Till the holy angels come,
And my eyes discern them,
Singing for the dying soul,
Requiem æternam."

—*Mediæval Latin Lyrics:*
translation, Miss Waddell.

In these centuries verse was the medium for medical teaching. Probably the earliest physician-poet was Floridus, who lived in France in the ninth century and wrote a lengthy collection of hexameters about the medical virtues of plants. The most famous poem of this type is the *Regimen Sanitatis* written at the medical school of Salerno about 1101, its author probably one John of Milan. This work was addressed to the lay public, was one of the earlier printed books in 1480, and has passed through over one hundred editions since then. As recently as 1922 an edition of Sir John Harington's English version was published in London.

This practice of using alliterative rhyming verse, particularly for works on domestic medicine was, of course, merely the result of classical tradition. The writing of verse by physicians, mostly epigrams and didactic epics, was common during Greek and Roman times. Nikandros of Kolophon (*circa* 133 B.C.), the son of a priest of Apollo, and himself a priest-physician wrote two works of poetry of considerable length dealing with bites of noxious beasts, antidotes and the virtues of herbs. Macer, in the third century A.D., wrote a materia medica in verse which was later commended by Linacre to his pupils. These are merely pedestrian examples of the practice which reached its highest expression in the work of the Roman poet, Lucretius (99-55 B.C.), whose philosophical poem *De Rerum Natura* is one of the great poems of the world. The only other didactic medical poem which we need consider is the poem *Syphilidis sive de Morbo Gallico tres libri,* published at Venice in 1530 and translated into English in 1686. Osler describes it as "the most successful medical poem ever written", presumably because it gave us the name of a disease. Its author, Girolamo Fracastoro (1483-1553), was born at Verona, became professor of logic at Padua, and afterwards practised medicine with great success. Like so many of his contemporaries he was an accomplished scholar, and was proficient in astronomy, natural philosophy, and poetry.

In search of our physician-poets we may pass at once to the sixteenth century. Ambroise Paré (1510-1590), a mighty figure in medical annals, wrote sonnets, and short verses appear in his various works, but he can hardly be ranked as a serious poet. In England there was an interesting group of poet-surgeons whose verse reflects the mediocrity of the time in literature. John Halle (1529-1568) published a poem in the metre of *In Memoriam,* entitled *The Court of Virtue Containing Many Holy or Spiritual Songs, Sonnettes, etc.* Thomas Gale (1507-1587), a prose poet whom Izaak Walton imitated, wrote *Certaine Works of Chirurgerie* and *Certain Works of Galen.* Thomas Vicary, the author of a work with the curious title *The Englishman's Treasure,* or *Treasor For Englishmen with the True Anatomye of Man's Body* (1585) wrote occasional verses. And John Read, an Elizabethan surgeon, wrote in metre *A Complaint of the Abuses of the Noble Art of Chirurgerie.*

The Golden Age of English poetry which began with Edmund Spenser's *Shepherd's Calendar* in 1579, and gave to the world the glorious varied plenty of Elizabethan poetry finds two physicians in the long bead-roll of famous names, each of whom has given us some of the loveliest lyrics in the language. These two men are Thomas Lodge and Thomas Campion. Thomas Lodge (1558-1625), the son of Sir Thomas Lodge, Lord Mayor of London, first tried his hand at law, then for a time was soldier, literary man, and later freebooter in the Spanish Main and the Brazils. He finally turned to medicine and graduated from Avignon and Oxford. He began practice in Warwick Lane, London, was successful as a physician, and continued to write. On May 11, 1604, he was examined at the Royal College of Physicians with a group of candidates which included Matthew Gwinne, Raphael Thorius, and the great William Harvey. He failed on that occasion, but was successful in 1609. The first two men mentioned in the above group are worthy of some slight degree of immortality as they celebrated in verse the delights of tobacco in the early years after its introduction into England, and were therefore among the first to establish for the profession of medicine that devotion to the ambrosial weed which has finely characterized it down the centuries. Thorius wrote the *Hymnus Tobaci,* while Gwinne, also a lesser poet, argued in its favour, in spite of the royal prejudice against it, at a medical disputation at Oxford for the edification, if not conversion, of James I in 1605. Lodge, in his practice of medicine, was somewhat of an authority on the plague, from which he died in 1625, nine years after the death of his greatest contemporary, William Shakespeare. It is Lodge's most famous work, *Roselynde, Euphues Golden Legacie,* that provided Shakespeare with his material for *As You Like It.* Lodge's chief volume of verse was *Phyllis* (1593), which contained some forty sonnets and lyrics and a long narrative poem. He is remembered by his little songs and madrigals, two or three of which, such as *Rosalind's Madrigal,* still find a place in every anthology of English verse. His lyrics have the limpid beauty characteristic of all the songs of the time, chastened at times by the poignancy of the uncertainty of life, for *Carpe diem* was the theme of men living in a time when even the highest or most brilliant were apt to meet death on the scaffold. So we find Lodge writing—

"Pluck the fruit and taste the pleasure,
Youthfull lordlings of delight;
Whilst occasion gives you seizure,
Feed your fancies and your sight:
After death, when you are gone,
Joy and pleasure is there none."
—From *Robert, Second Duke of Normandy*, 1591.

Master Thomas Campion (?–1619), poet, musician and doctor of medicine, (or "doctor in phisicke" as he was styled) was born about the middle of the sixteenth century, the precise date and place being unknown. Like Lodge, he was first of all a student of law in London, later turning to medicine and graduating from Cambridge. He had a most successful practice in London, and was a cultured, urbane man, with a wide circle of friends. His first book was a collection of Latin epigrams. He later wrote masques for presentation at court which are among the finest of their kind, a volume of songs on the death of Prince Henry, and four *Books of Airs* containing songs and lyrics, many of which were set to music by Campion himself. Campion has provided us with one of the strangest and most delightful surprises in English literature. His work was entirely forgotten until about forty-five years ago, when Mr. A. H. Bullen rescued it from oblivion, and since that time Campion's fame has grown steadily. His lyrics are perfect and exquisite examples of their kind, completely satisfying the relationship between music and poetry. To fully appreciate the beauty of his words, one must hear them sung to their music. Probably the best known of his songs is the one begining,

"There is a garden in her face,
Where roses and sweet lilies grow."

In another of his songs there occurs one of the most beautiful lines in our language. It is the last line of this stanza:

"Shall I come, sweet Love, to thee,
When the evening beams are set?
Shall I not excluded be?
Will you find no feigned let?
Let me not, for pity, more
Tell the long hours at your door."

One of his sonnets, in its astringent dramatic quality, has a curiously modern flavor.. It is addressed to a coquette.

"When thou must home to shades of underground,
And there arrived, a new admired guest,
The beauteous spirits do engirt thee round,
White Iope, blithe Helen and the rest,
To hear the stories of thy finished love
From that smooth tongue, whose music hell can move:
Then wilt thou speak of banqueting delights,
Of masks and revels which sweet youth did make,
Of tourneys and great challenges of knights,
And all these triumphs for thy beauty's sake.
When thou hast told these honours done to thee,
Then tell, O! tell, how thou didst murder me."

Poems expressing religious aspiration are seldom more than mere verse, but one such of Campion's beautifully unites expression and sentiment. It is included in Lewis Hind's anthology of the one hundred best poems in our language.

"Never weather-beaten sail more willing bent to shore,
Never tired pilgrim's limbs affected slumber more,
Than my weary spright now longs to fly out of my troubled breast.
O! come quickly, sweetest Lord, and take my soul to rest.

Ever blooming are the joys of Heaven's high Paradise.
Cold age deafs not there our ears, nor vapour dims our eyes;
Glory there the sun outshines, whose beams the blessed only see.
O! come quickly, glorious Lord, and raise my sprite to Thee."

Thomas Campion is certainly of the select few among the great poet-physicians.

Abraham Cowley (1618-1667), a native of London, scholar of Trinity College, Cambridge, and later of Oxford, spent his earlier years in the Royalist cause, living for a time in France as secretary to the exiled Queen Henrietta Maria. He was created in 1657 a Doctor of Medicine at Oxford by the Archbishop of Canterbury, by virtue of an ancient right which this office still possesses. He applied for the mastership of the Savoy hospital, but this was not granted. Finally, after the Restoration, a competence was provided for him by the Earl of St. Albans and the Duke of Buckingham and he retired from public life to the country. He does not appear to have practised medicine. He was, however, an original member of the Royal Society and published a Latin poem on plants. During his lifetime he was regarded as the greatest English poet and on his death was buried in Westminster Abbey. His fame quickly waned; indeed, there is a melancholy note in Cowley's writing about himself, for, while fortune treated him rudely, he never really fulfilled the promise of his youth. He had been an amazingly precocious boy, writing poetry at the age of ten, and publishing his first work when fifteen. Later he set the contemporary fashion of writing poetry, and in literary history is remembered as one of the first to establish what may be termed the modern prose style. In 1737 Pope wrote of him:—

"Who now reads Cowley? If he pleases yet,
It is his moral pleases, not his wit;
Forgot his epic, nay, Pindaric art,
But still I love the language of his heart."

The language of Cowley's heart is in his prose and there is little in his poetry that merits quotation in these days.

The next figure, Henry Vaughan (1621-1693), is one for whom poetry is deeply in debt to medicine. Vaughan, the "Silurist", as he was called because of his native place among the Silures in the county of Brecknockshire in South Wales, was educated at Jesus College, Oxford, and was a staunch Royalist, being imprisoned for a time during the Civil War. He

practised medicine in his native town and achieved a considerable reputation. His literary work was an avocation pursued for the love of writing and for the opportunity it gave him to express a singularly religious and mystical nature. During a long life he remained aloof from the turmoil of the world, and in genuine humility of aim and spirit he achieved immortality. It is of interest that he had a twin brother, Thomas, who was also a poet and a famous Rosicrucian. Both brothers have places in the Dictionary of National Biography, two twins thus achieving fame apparently being unique in history.

Vaughan's great poems are contained in the volume entitled in quaint classical fashion—*Silex Scintillans, or Sacred Poems and Private Ejaculations.* His poem *The Retreate* provided Wordsworth with some part of his inspiration for the famous *Ode on the Intimations of Immortality.* Some half dozen of his poems are the finest expression in our language of spiritual aspiration. As a writer of religious verse he is of the company of George Herbert and John Donne. If there is a question as to the finest poem ever written by an active practising physician, there is no doubt at all that the choice would be Vaughan's magnificent elegaic stanzas for departed friends beginning:—

"They are all gone into the world of light!
And I alone sit lingering here;
Their very memory is fair and bright,
And my sad thoughts doth clear."

Two other poems which gleam with the lights of magic phrases are *The World* and *Peace.* The imagery of the opening stanza of *The World* is superb:—

"I saw Eternity the other night
Like a great Ring of pure and endless light,
All calm, as it was bright,
And round beneath it, Time in hours, days, years
Driv'n by the spheres
Like a vast shadow moved, in which the world
And all her train were hurl'd . . . ."

Contrast this with the calm fervor of *Peace*:—

"My Soul, there is a Countrie
Far beyond the stars,
Where stands a winged sentrie
All skilfull in the wars.
There above noise, and danger
Sweet peace sits crown'd with smiles,
And one born in a Manger
Commands the Beauteous files . . . ."

The spirit of Vaughan is best expressed in the Latin inscription which he wrote to be placed on his tomb: "An unprofitable servant, the chief of sinners I lie here. Glory be to God! Lord have mercy upon me."

Two lesser names complete the roll of seventeenth century poet-physicians. Martin Llewellyn (1616-1682), scholar and cavalier, fought for the Royalist cause and afterwards practised in London. Later he became a Fellow of the Royal College of Physicians, and with the Restoration he was made physician to Charles II and Principal of St. Mary's Hall, Oxford. After four years he settled at High Wycombe where he practised till his death. His best known work was *Mere Miracles.* A number of his poems were satirical, and one of the last *Wickham Awakened,* or the *Quaker's Madrigal,* written in rhymed doggerel, was an attack on a Quaker rival who had annexed much of his practice. Francesco Redi (1626-1697) was a student of Pisa and physician to the dukes of Tuscany. In his scientific work he is regarded as the founder of comparative helminthology, and did much to refute the theory of spontaneous generation. He was a distinguished poet in his day, publishing *Bacco in Toscane, Arianna Inferma* and other works.

With the single exception of Goldsmith, the physicians of the eighteenth century produced little poetry of worth. They were men who in the custom of the time wrote verse of a sort, much of it polished, but little memorable. They talked and drank with the wits in the coffee houses, and certain of them were members of the reigning literary circles of the time. As Sir Edmund Gosse has pointed out, these friendships forged the abiding ties between literature and medicine which have persisted to our day and have found their modern expression in the figure of the late Poet Laureate, Robert Bridges.

To use Gosse's figure, the last embargo dividing literature from medicine was broken down by Sir Samuel Garth (1659-1718), a distinguished member of the Royal College of Physicians and a Harveian and Galstonian orator. Known as the "Kit-Kat Poet", he was a friend of the leading literary and political men of the age—Addison, Steele, Walpole, Halifax and Marlborough. Pope called him "the best of Christians without knowing it" and Dr. Johnson, always the master of the telling phrase, said of him that no man knew his art more or his trade less. His mock-heroic poem *The Dispensary* ridiculed the apothecaries and those physicians who opposed the establishment of a dispensary where the poor could get advice from the best physicians. The poem is celebrated less for its verse than for its recognition of the claims of literature and medicine on an equality of importance. In 1700 Garth pronounced the funeral oration over John Dryden, the laureate, as the body lay in state in the hall of the Royal College, and was present when it was buried in the Poets' Corner in Westminster Abbey. This oration of Garth's, it should be added, caused something of a scandal by its fulsome praises of Apollo and the classical ideals and its rather scant references to Christianity — the ever-recurring voice of the medical pagan!

Erasmus Darwin (1731-1802), grandfather of Charles Darwin, practised medicine successively at Nottingham, Lichfield and Derby. In his fiftieth year he wrote a long poem called *The*

Botanic Garden. Another of the lesser versifiers was John Armstrong (1709-1779), a Scot, and a rather splenetic gentleman, whose first poem *The Oeconomy of Love* created something of a stir, one commentator writing that he hymned the praises of Venus in strains so warm that they dissolved away his practice." He later atoned for this error with the didactic poem expressing, with the utmost medical decorum, *The Art of Preserving Health.*

John Wolcot (1738-1819), who wrote under the pseudonym of Peter Pindar, figured in some of the literary quarrels of the day. He had great satirical ability, but his humour at times was rough and libellous, while his verse resembled the slashing surgery of his time. In the literary battles which gave spice to this century a lone figure, attacked by both the medical and literary camps, was Sir Richard Blackmore (1653-1729), who had graduated in Arts at Oxford and in medicine at Padua, and was physician to William III and afterwards to Queen Anne. He was a prolific writer and it was said:

"In leisure hours in epic song he deals,
Writes to the rumbling of his coach's wheels."

His poem *Satyr against Wit* brought on his head the stinging couplets of a band of literary enemies, including Dryden, Pope, Steele and Garth. While in his own day Blackmore was praised by Dr. Johnson for his philosophical poem *The Creation,* the judgment of posterity is with Gosse, who dryly remarks that as an epic poet not even Phoebus Apollo can resuscitate him.

Another figure whose eminence in medicine far outstrips his ability in verse is Mark Akenside (1721-1770), the son of a Newcastle butcher, who graduated as Doctor of Physic at Leyden and later became physician to the Queen and a Harveian Orator. Wealth came to him suddenly through the bequest of a certain Jeremiah Dyson who gave him a house, an allowance, a chariot, and considerable advertisement. His principal work *The Pleasures of the Imagination* is a long didactic poem in blank verse. He also wrote many odes in the manner of Gray and Collins. His arrogant manner made him many enemies, and probably on this account he was satirized by Smollett in *Peregrine Pickle.*

(To be continued)

Association Notes

Report of Meeting of the Executive Committee

The Executive Committee of the Canadian Medical Association met in the Chateau Laurier Hotel, Ottawa, on Thursday and Friday, October 29 and 30, 1936.

The following members of the Committee were present:

Dr. Hermann Robertson, Victoria; Dr. Geo. S. Young, Toronto; Dr. A. T. Bazin, Montreal; Dr. J. E. Bloomer, Moose Jaw; Dr. W. K. Colbeck, Welland; Dr. Léon Gérin-Lajoie, Montreal; Dr. J. C. Gillie, Fort William; Dr. Duncan Graham, Toronto; Dr. A. S. Kirkland, Saint John; Dr. T. H. Leggett, Ottawa; Dr. K. A. MacKenzie, Halifax; Dr. W. J. P. MacMillan, Charlottetown; Dr. D. S. Macnab, Calgary; Dr. J. C. Meakins, Montreal; Dr. H. H. Milburn, Vancouver; Dr. E. S. Moorhead, Winnipeg; Dr. A. G. Nicholls, Montreal; Dr. F. S. Patch, Montreal; Dr. G. Harvey Agnew, Toronto; Dr. T. C. Routley, Toronto.

The Chairman, Dr. Geo. S. Young, presided.

A large number of items engaged the attention of the Committee during its two-day session. Reference will here be made to some of them.

The Executive Committee expressed to the President and Mrs. Robertson the very deep sense of appreciation of the profession for their kindness in visiting Eastern Canada and several of the other provinces during the autumn months.

ANNUAL MEETING, 1937

The President-Elect, Dr. T. H. Leggett, reported excellent progress in connection with arrangements for next year's annual meeting which takes place in Ottawa during the week of June 21st. Committees have been appointed to deal with the many aspects of the meeting. All are hard at work. The sessions will be held in the Chateau Laurier Hotel where excellent accommodation has been arranged. As this is to be a joint meeting with the Ontario Medical Association, a large attendance is anticipated.

RADIOLOGICAL SECTION *re* COLLEGE OF RADIOLOGY

The Radiological Section reported that it desires steps to be taken as soon as possible to establish standards of qualifications for Radiologists and expressed the belief that this might be accomplished by the setting up of a Canadian College of Radiology. The opinion was expressed in the Executive Committee that some action should be taken by some authority not only in respect to radiology but to the other specialties as well. It was felt by the Committee that the Royal College of Physicians and Surgeons of Canada, with the cooperation of the Canadian Medical Association, might be the proper body to undertake this duty and it was

so recommended. Subsequently at the annual meeting of the College, the proposal was approved. It would now appear that definite progress may be looked for in meeting the requirements which, in recent years, have been keenly discussed by a number of our Sections.

COMMITTEE APPOINTMENTS

Osler Memorial Committee — Dr. W. W. Francis, of Montreal, was named Chairman, succeeding the late Vaughan Black of Moose Jaw.

Committee on Education—Dr. F. J. H. Campbell, London.

Committee on Legislation—Dr. C. J. Veniot, Bathurst, N.B.

Committee on Nutrition—Dr. J. C. Meakins, Montreal.

MEDICAL ECONOMICS

It was stressed at the Victoria Meeting that the subject of Medical Economics is one of the most important before the Association. Following very careful consideration, the Committee expressed the opinion that the officer acting in a secretarial capacity in the field of medical economics should be thoroughly conversant with varying conditions of medical practice throughout Canada; that medical economics is a subject whose importance in the next ten years might be found to dwarf other activities of the Association; and that arrangements should be made to enable the General Secretary to assume the direction of the study of this question, and that he be free to travel to the assistance of any region of Canada requiring aid. Accordingly, the General Secretary was asked to assume this duty. Subsequently, the Directorate of the Ontario Medical Association appointed a full time assistant secretary for that Province in the person of Dr. A. D. Kelly, of Hamilton, and it is expected that this appointment will make it possible for the General Secretary to devote the time required to the field of medical economics. The General Secretary was further instructed to visit the British Isles and Europe this coming winter for the purpose of obtaining first hand information regarding health insurance and allied projects in those countries.

HEALTH INSURANCE

Following discussion on the question of health insurance, the following resolution was passed:

"Whereas the subject of health insurance is of vital interest and importance to every member of the medical profession of Canada: and whereas the Province of British Columbia has during the past year enacted legislation providing for a plan of Health Insurance for the province; and whereas the medical profession of British Columbia in their relation to this problem are serving not only themselves but all the medical profession of Canada, be it resolved that this Executive Committee place itself on record as pledging the wholehearted support of the Canadian Medical Association to its Branch in British Columbia, namely, the British Columbia Medical Association, in order that the best interests of the medical profession as well as the public may be safe-guarded in the implementation of such legislation."

HISTORY OF THE CANADIAN MEDICAL ASSOCIATION

The members of the Association have been slow in purchasing this excellent volume dealing with the history of the Association from its inception up to more recent times. Provincial Associations are urged to cooperate in stimulating the sale of this book at the price of $3.00. It should be in the library of every member of the Association. Orders should be sent to the office of the General Secretary.

CANCER

Dr. J. S. McEachern, of Calgary, Chairman of the Canadian Medical Association Study Committee on Cancer, was authorized, in his capacity as member of the Trustee Board of the King George V Silver Jubilee Cancer Fund for Canada, to support the establishment of a national organization to deal with the subject of cancer, and, further, to proffer to the trustees the wholehearted support of the Canadian Medical Association in doing everything which naturally comes within the purview of the Association to combat cancer.

RADIO

Your Committee was informed by the radio authorities that many listeners throughout Canada complain that reception is interfered with by electric equipment used by the medical profession and others. A special committee was appointed to confer with the radio authorities in respect to this matter. The committee has met and reports progress looking to a solution of the problem.

With respect to the question of radio continuities of an alleged health character, it was pointed out that, despite the excellent work being done by the Department of Pensions and National Health in censoring this material, there is still much going over the air relating to quackery, and misinformation in the health field. A special committee to deal with this matter was appointed under the Chairmanship of Dr. C. J. Veniot, M.P., of Bathurst, N.B.

MEMBERSHIP

Our membership and subscriptions for the year 1936 stand at 3,671, which is a gain of 698 over the previous year.

Considerable discussion took place with regard to a composite fee being established as a forward step towards federation. Three provinces, namely, Nova Scotia, New Brunswick and

Ontario undertook to canvass the situation immediately with regard to the possibility of giving practical effect to the suggestion in the coming year.

HOSPITAL SERVICE DEPARTMENT

Dr. Agnew reported splendid progress all along the line with respect to the work of his Department which endeavours to serve the hospitals and the medical profession, always keeping in mind the fact that the hospital is the workshop of the doctor, which gives him a very definite interest in hospital management.

FEDERATION

Dr. W. K. Colbeck, Chairman of the National Committee on Federation reported progress. All the provinces have appointed study committees and their representatives on the Executive Committee reported as follows:

Nova Scotia—DR. MACKENZIE. A questionnaire on the subject of federation was sent out to every doctor in the province. The response was very satisfactory. The Nova Scotia Medical Society at its last annual meeting in September of this year, passed the following recommendations:

"1. That this Society reaffirm its endorsation of the principle of federation, provided that a scheme can be evolved with satisfactory definitions of the powers and functions of the federal and provincial bodies.

2. That, in view of the legislative enactments required in Nova Scotia, and in view of the necessity of further elaboration of the scheme, this Society should defer completion of federation at this time.

3. That this Society appoint a study committee as requested by the Canadian Medical Association for collaboration with its sub-executive in further study of this matter; and that Dr. K. A. MacKenzie, a member of the Canadian Medical Association Executive, be Chairman of this study committee.

4. That this study committee be empowered, at its discretion, to employ legal counsel in the preparation and completion of the necessary legislative amendments."

Nova Scotia is now ready for a composite fee of $15.00 while federation is being studied further. Upwards of 250 doctors in the province out of a little over 400 are willing to pay this fee. Nova Scotia is in favour of federation and the province is not very far away from it. After the matter has been clarified and some minor difficulties are removed, Nova Scotia may be counted upon to enter federation.

Prince Edward Island—DR. MACMILLAN. Prince Edward Island is wholeheartedly in favour of federation and is prepared to guarantee 50 per cent of its medical registrants as members. The association feel that they would be losing nothing in changing their name to the Canadian Medical Association, Prince Edward Island Division, but rather that they would be gaining.

New Brunswick—DR. KIRKLAND. Federation has been carefully studied in this province. New Brunswick has a composite compulsory fee of $7.00. It would be impossible to bring 100 per cent of the medical profession of New Brunswick into federation. It would be a hardship to ask some of the men to do this. New Brunswick might safely guarantee 50 per cent of its registrants in federation, and any attitude of criticism of the proposal which the province once had would now appear to have changed to approval.

Quebec—DR. PATCH. The question of dual language in Quebec naturally presents difficulties. Our *Journal* is not widely read by our French Canadian colleagues. There is, however, a great deal of interest in Quebec in respect to the proposal. It would be impossible to guarantee any number of members but the situation is being canvassed in Quebec and we may look for progress in the future.

Dr. Gérin-Lajoie concurred in Dr. Patch's remarks.

Ontario—DR. GILLIE. There now appears to be a widespread swing in Ontario favourable to federation. Some changes should be made in the constitution and by-laws for Divisions but I think these are minor in character and in no way interfere with the principles and fundamentals underlying the plan. Compulsion should never be allowed to enter into the proposal. The Ontario Medical Association may be counted upon, when the matter is completely and thoroughly understood by its members, to move in the right direction with respect to unity in the medical profession.

Manitoba—DR. MOORHEAD. Dr. McKenty has undertaken to act as Chairman of the Committee on Federation in this province. He reports progress. He is approaching the question from its very foundations and believes that any structure which we build must be acceptable to the profession as a whole across Canada. Thus, we must begin at the bottom and clear away any difficulties which may appear to be in the way. Federation is an ideal but we must build securely.

Saskatchewan—DR. BLOOMER. Saskatchewan has suffered tremendously during the past several years of economic depression. Twenty to 25 per cent of the practitioners of the province could not reasonably be expected to pay an increased fee at this time. Saskatchewan however, recognizes the advisability of federation of the medical profession and, with returning prosperity, may be counted upon to play its part.

British Columbia—DR. MILBURN. In 1934 and again in 1935, the Association expressed its

approval of the principle of federation. Since that time, health insurance has bulked so largely on the horizon of the medical profession of the province that federation has had to take second place. British Columbia believes that federation is desirable. We recognize fully the necessity of national unity.

Alberta—DR. MACNAB. Federation has become an accomplished fact in Alberta. We are now the Canadian Medical Association, Alberta Division. Alberta does not fear any interference in its affairs from outside the province. Clause 14 of the national Constitution leaves no doubt that each provincial division has complete autonomy over its own affairs. Our annual fee is $20.00 and the profession have responded admirably to the payment of same.

In summarizing, Dr. Colbeck, Chairman of the National Committee, felt that the reports from the nine provinces were very encouraging indeed, and that the profession as a whole across Canada were definitely working towards the goal of federation.

FEDERAL RELIEF

The Committee instructed that representations be made to the federal authorities that payment for medical services should be included in drought areas, particularly in Western Canada, where the Federal Government is providing all or the major portion of general relief. This matter has already been taken up with the authorities at Ottawa.

MENTAL HYGIENE SURVEY

An International Committee has been established to offer its services to any part of Canada where, in the opinion of the authorities a mental hospital survey seems desirable. Dr. B. T. McGhie, of Toronto, Deputy Minister of Health for Ontario, was appointed to represent the Association on this committee.

Many other matters were dealt with and referred to the appropriate committees.

It was the opinion of your Executive Committee, every member of which was present, that two days of very profitable and useful discussion had taken place.

All of which is respectfully submitted.

T. C. ROUTLEY,
General Secretary.

"Throw out opium, which the Creator himself seems to prescribe; throw out a few specifics which our art did not discover, and is hardly needed to apply; throw out wine, which is a food, and the vapours which produce the miracle of anæsthesia, and I firmly believe that if the whole materia medica, as now used, could be sunk to the bottom of the sea, it would be all the better for mankind—and all the worse for the fishes."

—Oliver Wendell Holmes.

Hospital Service Department Notes

Air-Conditioning in Hospitals

The application of "air-conditioning" to hospitals received considerable discussion at the recent Cleveland meeting of the American Hospital Association. The Committee on Air-Conditioning reported some eighty known hospital installations, the total number being estimated at not more than two to three hundred. The major interest would seem to be in the warmer States, and there emphasis was placed upon cooling and dehumidification, whereas in the northern areas winter humidification was a primary consideration. Many limit the installations to the operating rooms, delivery suites, or to special departments. The value of air-conditioning for various conditions was endorsed by several hospitals, favourable results being reported for the treatment of asthma, respiratory infections, sinusitis, cardiac conditions, prematurity, and the post-operative state. The lessening of surgical risk by adequate air-conditioning was stressed by one competent observer; it minimizes the loss of body fluids before, during, and after operations; lessens shock and other surgical hazards. To be most effective, the patient should have conditioned air not only while in the operating room but in the pre-operative and post-operative periods. In cooling rooms maximum benefit would seem to be achieved in temperate zones by limiting the difference between inside and outside temperatures to not more than 10 to 12° F. The mistake of overcooling, so frequently noticed in some theatres, is liable to cause chilling of an actively functioning skin and prove harmful rather than beneficial. Experiments have indicated that, where the air is dehumidified, the temperature on hot days need not be dropped more than 5° F. to give comfort.

In northern climates the greatest need is for humidification during the winter months. This is not only desirable for general health reasons in living quarters, but in the case of the prairie or northern hospital would seem almost necessitous because of the danger of static explosions in the operating room. How serious this danger really is and to what extent ordinary methods of humidification can counteract this menace are difficult to estimate. When one considers the frequency of contact sparking on cold days, particularly in certain of our provinces with high altitudes it is surprising that anæsthetic explosions are not more frequent than they are. As publicity of such accidents is avoided as much as possible, many hospital people feel that minor explosions are more frequent than reports would indicate. Fifty-five per cent

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

relative humidity in the operating room is considered to be the optimum state by the Committee mentioned above. This would minimize the explosion hazard and would not be too uncomfortable for the surgeons and nurses. The nursery may be humidified to a higher extent, particularly the prematurity room which needs high humidification.

Apparently the high cost of installation and of operation of really efficient systems is still a marked deterrent to the wider use of air-conditioning. On a large scale it is not economically feasible at the present time. In the discussion, Prof. C. A. Mills, of Cincinnati, the well-known authority on air-conditioning, pointed out that recent research has emphasized the objective to be that of conditioning the patient rather than the whole physical environment. Radiant heat would seem to have real possibilities in this respect, it being possible by this means to keep a person quite comfortable in a temperature many degrees below that usually considered necessary. In another report a Committee on Hospital Planning and Equipment stated that the two costly factors in air-conditioning, cooling and dehumidification, can be provided at a practicable cost for the operating and delivery rooms by small additions to the domestic refrigerating compressor capacity.

Recirculation of conditioned air has been criticized because of odours and the potential danger of bacteria dissemination. Partial recirculation is a distinct economy, provided it is not obnoxious or dangerous. One large hospital with 96 private rooms on a single unit reports 50 per cent recirculation to be satisfactory. This percentage would appear to be the average choice. Tests in one institution revealed that the passage of air through glass wool oil-impregnated filters reduced the average bacterial content of the normal air by some 60 per cent. "A recent development of major significance," according to the Committee on Hospital Planning and Equipment, "is the use of ultra-violet rays for destroying air-borne pathogenic bacteria in operating rooms and killing microorganisms that ruin meat, bread, cake, etc., in refrigerated store rooms."

DIAGNOSTIC WISDOM.—"(*a*) When physicians are discussing whether the case is appendicitis or not; it is. (*b*) When they are inclined to admit the possibility of appendicitis, without being perfectly sure of it; it not only is but it is about to perforate. (*c*) When the diagnosis is sure, there is already perforation, with a more or less circumscribed peritonitis."—Bastianelli.

Medical Societies

The Royal College of Physicians and Surgeons of Canada

The Sixth Annual Meeting of the Royal College was held in the National Research Council Auditorium, Ottawa, on Saturday afternoon, October 31, 1936, with a registration of ninety-five Fellows. The Council of the College had met throughout the forenoon for the transaction of business.

The program consisted of three parts—Scientific Session, Business Meeting, Convocation. The President, Dr. A. T. Bazin, presided.

In the Scientific Session the following papers were presented: "Some changing views about œdema and diuresis", Professor Henry Christian, Professor of Physic, Harvard University, Physician-in-Chief to Peter Bent Brigham Hospital; "Some factors in the development of cancer in mice", Professor C. Leonard Huskins, Professor of Genetics, McGill University; "Gastroscopy, its indications and value", Dr. Paul H. Thorlakson, Winnipeg.

After a short recess the business was proceeded with.

With the assembly standing the Honorary-Secretary, Dr. W. S. Lyman, read the list of Fellows deceased during the past year:—

Dr. Campbell Palmer Howard, Montreal, June, 1936;

Dr. O. A. Gagnon, Montreal, 1936;

Dr. N. J. Fiset, Quebec, August, 1936.

The President presented the report of Council activities for the past year. In abstracting this report it is noted that His Majesty King Edward has been pleased to graciously confer upon the College His Royal Patronage, an office previously adorned by His illustrious father.

An invitation from the Royal Australasian College of Surgeons to the annual meeting of that body in Auckland, New Zealand, during January, 1937, was received and all the Fellows were notified. It is hoped that one or more Fellows will be able to attend.

Council is of opinion that before this College can be *favourably* known it must be *better* known. To that end the Committee on Publicity has had appear in each issue of the *Canadian Medical Association Journal* and *L'Union Médicale* full page advertisements or announcements, as well as special articles reporting the meetings of Council. The same procedure has been followed in regard to Medical Undergraduate Journals, where available, *viz.*, McGill, Toronto, Western and Manitoba. Efforts have been made to interest the deans and professors of all medical schools in Canada, and meetings have been arranged with the undergraduate bodies.

A circular letter was issued to 57 hospitals comprising the list of those approved and recommended for internships by the Canadian Medical Association. This letter requested co-operation to the extent that, other things being equal, a candidate for internship who held a certificate of having passed the Primary Examination of this College, or its equivalent, would be given the preference of appointment. This letter has met with very favourable reception, only two of the fifty-seven finding it impossible to comply.

The Committee on Examinations, Applications, and Credentials reported that there were 28 candidates for the Primary Examination of whom 17 were successful; 4 candidates for the Final Examination in the Division of Medicine, of whom 2 were successful; and 10 candidates for the Final Examination in the Division of Surgery, of whom 3 were successful.

The names of the successful candidates follow: —

Primary Examination.—Dr. W. S. Anderson, Toronto; Mr. J. H. Belton, Toronto; Jacques deL. Bourgeois, Montreal; D. H. Capp, Toronto; H. Fine, Toronto; W. B. Gibson, Western; A. L. Gordon, McGill; F. M. Gurd, McGill; H. Hayward, Toronto; F. L. Lawson, Toronto; Louis Lefkovitz, Toronto; J. C. McCulloch, Toronto; J. C. Rathbun, Toronto; A. M. Swadron, Toronto; F. B. Thompson, Toronto; W. G. Trap, McGill; D. M. Whitelaw, McGill.

It is interesting to note that among the names on the above list are those of the sons of both the present Vice-presidents of the College.

Final Examination.—Medicine: Dr. J. A. Dauphinee, Toronto, University of Toronto; Dr. John E. Plunkett, Ottawa, Queen's; Surgery: Dr. D. E. Cannell, Toronto, University of Toronto; Dr. H. F. Robertson, Toronto. University of Toronto; Dr. H. R. Ziegler, Toronto, University of Toronto.

Ad Eundem Fellowship in the Division of Surgery was granted to Dr. Harry Stafford Morton, Halifax, his qualifications being B.A., M.Sc., M.R.C.S., L.R.C.P., M.B., B.A., London, F.R.C.S. England.

Council is very seriously considering the grave problem of expense to candidates, especially for the Primary Examination. Under the present system, although a great improvement over the earlier years, the candidate, otherwise well qualified, is unable, in many instances, to finance the transportation, maintainance and fees. The Council hopes to solve this problem without in any way lowering standards or relinquishing control.

NOTE.—This report will be completed in our next issue.—[ED.]

University Notes

The University of Western Ontario

The following appointments and promotions in the Faculty of Medicine are announced. *Appointments.*—Mr. A. J. Grace, B.A. (Sask.), M.A., B.M., B.Ch. (Oxon.), F.R.C.S. (Eng.), has been appointed Instructor and Fellow in Surgery. Mr. Grace began his medical education at the University of Saskatchewan whence he proceeded to Oxford as a Rhodes Scholar in 1926. At Oxford he had the distinction of obtaining a first in the final examinations in the honour school of physiology. After serving for two years as demonstrator of physiology at the Guy's Hospital Medical School, he held house appointments at Guy's Hospital for 18 months. He then joined the resident staff of the Royal Victoria Hospital, Montreal, where he spent 15 months. Following seven months as assistant surgeon at the Humber Clinic, Corner Brook, Newfoundland, Mr. Grace returned to England to take over the duties of Resident Surgical Officer at the Radcliffe Infirmary and County Hospital, Oxford. In July, 1936, he received the appointment of Surgical Registrar at Guy's Hospital, London, England, which post he relinquished to come to London, Canada.

G. W. Stavraky, M.D. (Odessa), M.D., C.M., M.Sc. (McGill), has been appointed Lecturer in Physiology in succession to Dr. J. K. W. Ferguson, who has joined the staff of the Ohio State University at Columbus, Ohio. Dr. Stavraky, after graduating from the University of Odessa in Russia, and after completing a surgical appointment of one year there came to Canada in 1930. He engaged in research work with Prof. B. P. Babkin in the Department of Physiology at McGill University, and subsequently spent three years as Fellow in Physiology, under Prof. Wilder Penfield at the Neurological Institute, Montreal. Following this, he acted as Instructor of Physiology at McGill for one year.

G. W. Sumner, M.D. (Western Ontario), has been appointed Instructor in Pædiatrics. Dr. Sumner has completed three years' postgraduate training in Montreal and Cleveland.

Promotions.—Dr. G. H. Stevenson has been promoted from Associate Professor to Professor of Psychiatry; Dr. W. P. Tew, from Associate Professor to Professor of Obstetrics and Gynæcology; Dr. E. M. Watson, from Associate Professor to Professor of Pathological Chemistry; Dr. R. A. Waud, from Associate Professor to Professor of Pharmacology; Dr. D. W. Crombie,

from Instructor to Assistant Professor of Medicine, and Dr. P. M. Andrus, from Instructor to Assistant Professor of Radiology.

Special Correspondence

The London Letter

(From our own correspondent)

By far the most outstanding event in the medical world since last month has been Lord Nuffield's offer to Oxford University. In his presidential address at the Oxford Meeting, Sir Farquhar Buzzard outlined a type of centre, where medical men and women could be trained for a career in clinical research. There was sitting on the platform beside the President on the occasion of this address one who has already made many benefactions to Oxford medicine, and in a letter published recently Lord Nuffield offered one-and-a-quarter million pounds to produce just the type of enlarged medical school that was suggested by Sir Farquhar Buzzard. The full details of the scheme will have to be worked out when the University accepts the offer, but in his letter, Lord Nuffield deals with so many points and makes it clear that he does not wish the University to suffer in any way by any increased demands made upon other scientific departments by the new school. Thus has reality been given to an "ambitious dream", as it was called in the presidential address, and the future working out of the Oxford Post-Graduate Training and Research Centre will be looked forward to with the greatest of interest.

While nutrition is very much still the popular subject, an enterprising commercial undertaking (namely, the Gas Light and Coke Company of London), has produced an excellent cinematograph film, completely free from any advertising matter and presenting an excellent analysis of this great social problem. The general commentary is by Prof. Julian Huxley, who, in his position at the Zoological Gardens, finds that much more attention is given to the diet of animals in captivity than to the diet of children in this country. The film is free from exaggeration, does not deal with the horrors of starvation, but simply and plainly exposes the problems of the ordinary working-class home. The relationship between food deficiencies and economic circumstances needs little emphasis, but the way in which it is brought out in the film is restrained and completely convincing. The differences between energy-producing and protective foods are shown, and it should be possible for this film to do a tremendous amount of good, both in rousing the public conscience and in transmitting correct well-edited knowledge to all spectators.

A few years ago an organization called the National Birthday Trust Fund was founded, with the idea of securing for all mothers safe forms of anæsthesia in childbirth as were already available to those who could afford to pay for them. Various steps have been necessary in the campaign, such as investigations as to safe forms of analgesia which could be used by midwives, and then when this was satisfactorily established the Central Midwives Board had to be convinced of the wisdom of allowing a midwife to give any form of anæsthetic. All these steps have now been completed, and it is announced that the Central Midwives Board regards the administration by a midwife of gas and air by the modern type of apparatus for the purpose of producing analgesia during labour as treatment within her province. Certain conditions are attached to this permission concerned with the instruction of the midwife, the certification by a medical practitioner within a month of the confinement that the patient is fit for gas and air, and, thirdly, that someone else must be present during the administration. Difficulties about expensive apparatus are being steadily lessened, and it is suggested that a portable gas and air machine will shortly be available and fifty gallon gas cylinders can be supplied, collected and delivered at a flat-rate charge, which will very probably work out at a cost of just over two shillings per case.

The month of October is always full of introductory addresses when leaders of the profession address new, present, and past students in the different medical centres. The present-day trend of medical progress towards the psychological side, emphasized by Sir Maurice Cassidy in the October issue of *The Practitioner*, was well shown in Lord Horder's address to the Westminster Hospital gathering on "The Doctor as Humanist". From an outsider's point of view, Lord Iliffe, joint proprietor of a well-known London paper, made some interesting comments on the part that could be played by the press in furthering objects of preventive medicine. Lord Dawson, at Guy's Hospital, indicated the broadening of the doctor's horizon which now has to include physical education and training of the mind. Even more important than these introductory addresses during the past month is the Harveian oration before the Royal College of Physicians of London on St. Luke's day, this year being delivered on the day after by Sir Walter Langdon-Brown. This annual homage to the memory of William Harvey is one of the important medical ceremonies in London at this time of the year, and the orator for 1936 dealt with Harvey's background, sketching in outline something of the careers of those men whose philosophy must have influenced the great physician.

ALAN MONCRIEFF.

121 Harley St.,
London, W.1.

The Edinburgh Letter

(From our own correspondent)

Professor Crew, of Edinburgh, recently addressed the Annual Conference of Women Citizens Association on the subject of fitness for parenthood. He expressed the view that the time was fast approaching when men and women would have to prove their fitness in this respect. These were the days of the environmentalists. According to them all would be well if only housing and nutrition were improved. He agreed that these factors were of the greatest importance, but there was a definite limit to their influence. If one could choose one's parents one could thereby determine most of the things that one would be, and very largely most of the things that one would do. Heredity and environment, nature and nurture, were the forces that made and moulded personality. Heredity fixed the limits of the development of the individual; nurture permitted or encouraged development to take place, but on the other hand it could prevent, embarrass, or deflect it. He pointed out that the Eugenics Society had evolved a scheme which would make a voluntary pre-nuptial examination a very simple and profitable thing. The project, he was sure, was a step in the right direction, in the sense that it was meant to be purely voluntary—there were no certificates about it. It was, he thought, an intelligent anticipation of what would be in the not too remote future a compulsory scheme backed by law, for he was perfectly certain that the State was bound in its own interests sooner or later to place its sentinels at the portals of birth. He thought that the bounden duty of one generation was to insure that the social inheritance of the next should be so shaped that everyone in it should achieve the fullest degree of expression of his or her hereditary endowment. Measures were already being taken in Turkey, Norway, and Germany and in other countries to forbid the marriage of parents suffering from mental and physical diseases, and he believed that Britain in its own interests should adopt a system of pre-nuptial certification.

Professor Cathcart, of the Chair of Physiology of Glasgow University, in an address to the Scottish Association of Insurance Committees held at Greenock dealt with another aspect of eugenics. He referred to the falling birth rate and said there were two possible causes—a natural decline in the powers of reproduction or a wilful prevention of conception. It had been suggested that, quite apart from a possible decline in fecundity, the birth rate had fallen owing to economic circumstances, the age of marriage being postponed to a less fertile period. This possibility had been explored, and in Scotland at least it could be stated that the decline in the birth rate was not due to a postponement of the marriage age. All the evidence available showed that the decline was due to the wilful control of reproduction. Birth control might serve a very useful purpose in the proper spacing of births, but unrestricted birth control had become a national menace. The reasons underlying this were in part economic, in part social. It was highly improbable that any mere improvement in economic conditions would alter the present trend.

The increase in the consumption of medicines was recently the subject of comment by the Minister of Health. He stated that the total cost of prescriptions issued to insured persons in England and Wales had increased during the past twelve years from £1,325,000 to £2,100,000. This increase was out of all proportion to the increase in the insured population. Some part of it might be due to propaganda advising people to consult their doctor early, but the greater part was the result of the growth of the "bottle" habit. Insured persons were too apt to feel that they were not receiving proper treatment unless they got a prescription every time they saw their doctor. He was alive to the gravity of the problem, and he stated that the officers of the Ministry of Health were actively considering the situation in conjunction with the British Medical Association. It is of interest in this connection to note that the cost of medicines among the insured population of Scotland is very much less than it is in England. This may be due to better appreciation of the fact that the doctor's general advice may be of much more value in many cases than a prescription. Even so there is room for improvement. There may be some truth in the Minister of Health's comment that the doctor too often takes the easier line of giving a prescription, whether the patient really needs it or not. The fetish of the bottle dies hard.

Scotland recently suffered a severe loss by the death of Sir Godfrey Collins, Secretary of State for Scotland. He took a very active interest in all matters pertaining to the health of the people. He was responsible for the setting up in 1933 of the Departmental Committee on Scottish Health Services and he recently introduced in the House of Commons the Maternity Services (Scotland) Bill. His death at this juncture when the entire medical services are in process of review is much regretted. He took a great interest in the measures taken to improve the housing conditions of the people. His views as to the future lines of development of the medical services were characterized by foresight and a practical realization of what could be achieved.

R. W. CRAIG.

7 Drumsheugh Gardens,
Edinburgh.

Letters, Notes and Queries

Blood Pressure and Artificial Pneumothorax

To the Editor:

With reference to Dr. Farrell's letter in the November issue of the *Journal*, may I refer you to the article by Jerome R. Head on the "Effect of High Intrapleural Pressure on Blood Pressure", in the *Archives of Internal Medicine*, volume 56, number 5, pages 904-911. The author cites two cases of chest trauma with fluid and air in the pleural space. Both had high intrapleural pressures which resulted in a definite lowering of the blood pressure with a marked fall during inspiration. While the expiratory blood pressure was well above that usually productive of signs and symptoms of circulatory failure (shock), definite shock was present. The mean blood pressure evidently was below the critical level. In both cases lowering the intrapleural pressure by aspirating fluid raised the blood pressure, decreased the discrepancy between its inspiratory and expiratory phases, and brought about the immediate disappearance of the symptoms of circulatory collapse.

The author further gives a table listing the effects of changes in intrapleural pressure in artificial pneumothorax. The same discrepancy between the inspiratory and the expiratory blood pressure is observed in patients with pleurisy with effusion and with both spontaneous and artificial pneumothorax.

The observations and syndrome reported are of frequent occurrence and of real importance. In cases of pleurisy with effusion and of spontaneous and artificial pneumothorax the fall of blood pressure on inspiration indicates definite cardiorespiratory embarrassment, and a lowering of the blood pressure on expiration points to a condition which may rapidly lead to circulatory failure and death. It is important to know that even when there is an expiratory pressure of over 100 mm. of mercury the mean pressure may be below the critical level for shock. In cases of hæmorrhage into the pleural cavity it is important to know that both the loss of blood and the rising intrapleural pressure tend to lower the blood pressure and that the collapse incident to it may be immediately relieved by lowering the pressure in the pleural cavity.

The author is not dogmatic in his explanations but merely points out several physiological theories—a mechanical theory, a vasotonic theory and a neurogenic theory. In conclusion he says that high pressure in the pleural cavity acts directly on both the pulmonary and systemic circulation, on the former by collapsing the lung and on the latter by compressing the great veins.

Collapse of the lungs causes: (1) a decrease in the flow of blood through the collapsed lung; (2) a rise in pressure in the pulmonic circulation; (3) and increased strain on the right heart; and (4) a reduction in vital capacity. Compression of the great veins causes: (1) a rise in the venous pressure; (2) an insufficiency in the return of venous blood; and (3) a decreased output of the heart.

Up to relatively extreme degrees of pressure these hindrances are compensated for by an increase in tone of the vasoconstrictor centre. The first sign of the strain on this compensatory mechanism is an exaggeration of the Traube-Hering waves, a tendency for the peripheral resistance to give way during inspiration. A time comes when the centre can no longer fully compensate and the mean blood pressure falls below the critical level.

The above may not explain Dr. Farrell's question fully, but it certainly bears out his observations. I myself have noted patients receiving artificial pneumothorax to feel better after their refill. I have frequently heard a patient say "I feel the need for more pneumo". Thus, it seems to me also that there must be a mean level which gives the best tone in collapse therapy.

S. ADRIAN YAFFE,
Intern, St. Joseph's Hospital,
November 13, 1936. *Hamilton, Ont.*

Answers to letters appearing in this column should be sent to the Editor, 3640 University Street, Montreal.

Dr. Kline's Remedy

To the Editor:—

There is a propriety preparation on the market called "Dr. Kline's Remedy for Nervous Irritability and Excitability, Sleeplessness and Nervous Spasms of Epilepsy". Could you tell me what the ingredients of this mixture are, and if not where I could find out?

I am enclosing one of their order forms by which you will see that they manufacture quite a few preparations. I understand that their preparations used to be obtainable in Montreal, but now have to be ordered direct from Red Bank, N.J., U.S.A.

F. O. GALBRAITH.
Stettler, Alta.,
October 13, 1936.

Answer:—

The Bureau of Investigation of the American Medical Association has sent us the following note about this preparation. [ED.]

"This used to be sold under the name of Dr. Kline's Epilepsy Cure, put out by Dr. R. H. Kline, of Philadelphia. Later, it became Kline's Nerve Remedy, sold by the Dr. R. H. Kline Company, of New York City, and sent out from the same address as the Lexington Drug and Chemical Company, which exploited another 'epilepsy cure' known as Waterman's. The Dr. R. H. Kline Company used to declare

that it had its laboratories at Red Bank, N.J. This was the location of A. W. Chappell and his employee, H. W. Perkins, M.D., who sold Perkins' Favorite Prescription. Those that wrote to the Dr. R. H. Kline concern received a letter signed H. W. Perkins, M.D. There seems to have been a Dr. R. H. Kline many years ago, but he has long been dead. Dr. Kline's Nerve Remedy was analyzed by the Chemical Laboratory of the American Medical Association and found to be a bromide mixture, having identically the same composition as the product put out under the name, Dr. Waterman's Tonic Restorative."—*J. Am. M. Ass.*, March 6, 1915.

"The Country Doctor"

To the Editor:—

I wonder if you are aware of the film "The Country Doctor", which is running in this country at the present time? I saw it last night, and was greatly surprised that it should have passed the film censors here.

Conditions of medical service are shown in a very strange light, together with quite uncalled-for theatrical and dramatic touches. The doctor (presumably Dr. Dafoe, as the famous quintuplets arrive during the film) is portrayed by a strange mixture of Frenchman and a Jew; moreover, towards the end, he is discovered not to be in possession of a licence to practise. (If I were Dr. Dafoe, I should take action over this.) Moreover, why the strong Roman Catholic atmosphere in (presumably) Ontario?

I feel sure you would agree with me that the film is a caricature of Canadian life, and I should like to have your views on it. I am,

Yours sincerely,

JOHN S. MEIGHAN, M.B., CH.B.

Glasgow, Scotland,
October 20, 1936.

Topics of Current Interest

A Clinical Study of Abortion

A steady increase in admissions of abortions in some hospitals in England has occurred during the last ten years. Indeed, about 2 per cent of the total admissions in the general hospitals of the London County Council are cases of abortion. The deaths attributed to abortion in England and Wales in 1933 amounted to 24.2 per cent of the total deaths from puerperal sepsis.

In his recent review of 1,000 cases of abortion, Parish* found that 203 of the women had no living children and 173 were pregnant for the first time; 207 of these women had one living child and only 136 had six or more children. Admittedly, 485 of the women had induced abortion by one means or another, varying from the employment of an abortionist to the use of slippery elm bark. Most of the deaths that occurred in the entire series were in this group. In another group, of 246 cases, abortion was the result of various diseases or conditions, the most common, in order, being uterine displacement, accidents, pulmonary diseases, pelvic diseases, lacerated cervix and renal diseases. There was no intervention in this group, and there were no deaths. Of the 1,000 cases under review, infection was present in 48.3 per cent on admission to the hospital.

For the group of 151 cases of threatened abortion, the plan of treatment was to place the patients completely at rest, giving 0.016 gm. (one-fourth grain) of morphine if pains were present, and to defer pelvic examination if the diagnosis was clear. With this treatment 57 per cent of the patients with threatened abortion were discharged still pregnant. For the 148 cases of inevitable abortion no treatment other than ergot was given unless there was a special indication. If the abortion was not progressing, an enema was given followed by three injections of 0.5 c.c. of solution of posterior pituitary every two hours. When this treatment failed to complete the abortion the uterus was evacuated. In 72.9 per cent of the cases of inevitable abortion completion occurred spontaneously or with the assistance of drugs. Of 481 cases of incomplete abortion infection was present on admission in 52 per cent. Expectant treatment was followed until the fever subsided, unless hæmorrhage necessitated more active measures. Five days was found to be a satisfactory period to allow between the subsidence of fever and evacuation of the uterus. When the temperature, however, failed to return to normal in a week, the retained products were removed from the uterus with as little trauma as possible. If it was necessary to dilate, great care was taken not to split the cervix, to avoid any pathway for the entry of microorganisms into the parametrium. If the uterus could not then be evacuated digitally, a blunt curette was used only to explore the uterus. When drawn gently over the uterine surface, if an obstruction was located, a slightly firmer pressure was made to remove it, but curettage was not performed. The uterus was flushed with a mild antiseptic solution; when retained products ceased to come away with the flushings, the curette was abandoned.

Four hundred and sixty-one cases required operative intervention to evacuate the uterus completely, and 7.2 per cent of these later showed some rise in temperature, while in only 1.7 per cent of the spontaneously completed abortions was there any exacerbation of infection. Active infection was present in more than half of the cases of complete abortion on

* Parish, T. N., A thousand cases of abortion, *J. Obst. & Gyn. Brit. Emp.*, 1935, **42**: 1107.

admission to the hospital; if the temperature did not fall with bed rest in such cases, treatment by means of intra-uterine injections of glycerin was undertaken. All but one of the eighteen patients who died was infected at the time of admission; in the one fatal case, septicæmia became apparent six days after curettage for subinvolution.

The mortality rate for the entire series of 1,000 abortions was 1.8 per cent. Mortality from abortion is due chiefly to sepsis following illegal interference with pregnancy; it is therefore preventable.—*J. Am. M. Ass.*, 1936, **107**: 284.

Removing Adhesive Tape

The deaths of two football players at Purdue University and the serious burning of several others as a result of the explosion of gasoline focuses attention on the correct method of removing adhesive tape. From time to time, various recommendations have been made as to the easiest methods of performing this task. Every one knows that it is painful to turn up one edge of the adhesive tape and to jerk it suddenly away from the skin. Furthermore, this will pull out the hair—and even remove the skin—and give opportunity for secondary infection. Gasoline has been recommended in the past, as well as ether and various volatile oils. Kerosene has also been employed for removal of adhesive tape from the skin. None of these substances meet the optimal indications. For some time ethyl acetate was advocated, but it has a definite fire hazard and is irritating to the eyes, nose and throat. Carbon tetrachloride is known as a standard fire extinguisher. It is not inflammable and is frequently used for the removal of tape. It constitutes the chief ingredient of some of the well known cleaning fluids on the market. Recently the Council on Pharmacy and Chemistry has voted to accept[1] two solvent preparations proposed primarily for the removal of adhesive tape from the skin. One[2] of these substances consists of 98 per cent dichlormethane and has no fire hazard, since it is non-explosive and non-inflammable. However, it is similar to chloroform in its action and the same precautions are necessary as to its inhalation. The other product[3] is a mixture of approximately 60 per cent carbon tetrachloride and 40 per cent naphtha with a small amount of oil of sassafras. Such a mixture may burn but will not explode under ordinary conditions, and in the ordinary sense is considered to be non-inflammable. With any of these preparations there may be some danger associated with the removing of large quantities of tape in small rooms without proper ventilation. This is, however, a minor danger and should not be seriously disturbing. Certainly it is a far less hazard than the use of gasoline anywhere near a source of flame or heat. Coaches and trainers of football teams will do well to equip training quarters with plenty of modern improved solvents so as to eliminate the danger of catastrophe such as that which has thrown a sombre atmosphere about the current football season.—*J. Am. M. Ass.*, 1936, **107**.

1. Acceptance awaits receipt of properly revised advertising and labels to conform to the Council's decisions.

2. Dichlormethane Solvent-Belle, marketed by Belle Alkali Company, Charleston, W. Va.

3. Ohio Carbon Tetrachloride Compound, marketed by Ohio Chemical & Manufacturing Company, Cleveland.

Abstracts from Current Literature

Medicine

Chronic Hæmolytic Anæmia with Paroxysmal Nocturnal Hæmoglobinuria. Hamburger, L. P. and Bernstein, A., *Am. J. M. Sc.*, 1936, **192**: 301.

The authors report two additional cases of chronic hæmolytic anæmia with paroxysmal hæmoglobinuria, bringing the total of reported cases to 22. The patients, one a woman of 28, the other a man of 29, were both alive and in fairly good health at the time the paper was written. Both continued to have recurring attacks of hæmoglobinuria with fever, anæmia and jaundice in spite of all treatment, which included splenectomy in one case. The Donath-Landsteiner reaction was negative. The spleen removed in one case weighed 360 grams and was in other respects normal.

The clinical features of the disease are summarized as follows:—The urinary discoloration may occur during the day but usually comes on at night. It is due to the presence of hæmoglobin and methæmoglobin. Urobilin and hæmosiderin are also present. The signs and symptoms of the syndrome which appear with the hæmoglobinuria are variable. There are usually abdominal, lumbar and substernal pain, jaundice and fever. The disease may be differentiated from other forms of paroxysmal hæmoglobinuria in that the syndrome is not produced by chilling or by excessive exertion. It differs from hæmolytic jaundice in that there is no alteration in the shape or fragility of the erythrocytes, and usually no splenomegaly. The chief blood changes are an anæmia, which may become profound, reticulocytosis, and perpetual hæmoglobinæmia. The urine always contains urobilin and hæmosiderin. Therapeutic measures, including splenectomy, are of little avail, but the disease is compatible with life for many years. Transfusions are generally followed by untoward reactions accompanied by hæmoglobinuria.

The authors advance the theory that the malady may result from the absorption of some material from the gastro-intestinal tract acting

as an allergen or a hæmolysin. They further suggest that benign forms of this type of chronic hæmolytic anæmia may pass unrecognized when hæmoglobinuria is not a conspicuous feature.

E. S. MILLS

A Common Lesion of the Cervical Spine Responsible for Segmental Neuritis. Turner, E. L. and Oppenheimer, A., *Ann. Int. Med.*, 1936, **10**: 427.

This paper deals with a critical survey of over 50 patients with the common finding of a distinct and clear-cut narrowing of one or more of the intervertebral spaces of the middle and lower cervical spine. Most of the patients were over 50 years of age. Pain in some part of the shoulder girdle, arm, hand, back, præcordium, or neck was usually the chief complaint, and, next to pain, weakness in one upper extremity, or inability to perform certain movements. Most of the patients were not conscious of pain in the neck, and as a rule there was no restriction of neck movements, active or passive. Whenever a patient complained of exaggeration of pain on walking immediate relief was obtained by the wearing of soft rubber soles and heels. Pain over one shoulder was the most common of all chief complaints. Atrophy of the small muscles of the hand was present in some instances. When the atrophy is unilateral the condition is suggestive of an accessory cervical rib.

Although the types of spinal changes observed roentgenologically were variable, the one consistent finding in all cases was the narrowing of one or more of the intervertebral spaces in the cervical spine. This narrowing was found whether hypertrophic arthritis, infectious arthritis, or traumatic displacement was present in addition. This narrowing of the interspaces was present in some cases in which there was no evidence of "spicule" or exostosis formation. The authors believe that this narrowing may be the first change of importance that takes place in many or perhaps all of the cases that later develop hypertrophic spondylitis, the thinning of the intervertebral disc subjecting the vertebral bodies to trauma, especially along their margins. The authors believe these cases are quite common. If kept in mind, they will be seen from time to time in every physician's office. The treatment is traction and ultra-short-wave therapy to the cervical spine, and the wearing of soft-soled shoes.

H. GODFREY BIRD

Surgery

Technical Details in Skin Grafting. Conway, J. H., *Surg., Gyn. & Obst.*, 1936, **63**: 369.

The author reports the results obtained in attempting primary union of Davis "pinch-graft" skin defects. In 90 cases at the New York Hospital primary union was effective in every case without mishap. He attributes the excellent results to thorough asepsis and to the following procedures. If, where only a few grafts are required, they be taken in a vertical direction the defects can be closed by individual sutures and an interrupted straight-line cicatrix be obtained. In those cases where numerous grafts are essential it is advised that an ellipse of skin, not more than 3 to 4 cm. at its greatest width, be marked out with its greatest length vertical. The entire cutaneous surface within this ellipse can be utilized. The remaining subcutaneous tissue overlying the fascia can be removed, the skin generously undercut, the edges approximated by a subcuticular suture with dermal sutures for exact linear scar formation.

FRANK DORRANCE

Conservative Surgical Treatment of Carcinoma of the Penis. Nesbit, R. M. and Keitzer, W. O., *Surg., Gyn. & Obst.*, 1936, **63**: 504.

Since carcinoma of the penis is usually of low-grade malignancy, with metastases occurring, in Dean's series, about 33 months after the onset, in the external, iliac and pelvic lymph nodes as well as in the superficial iliac nodes, any involvement of less than the distal half of the penis calls for simple amputation 1.5 to 2 cm., proximally. Infection should be allowed to subside before regional gland dissection is carried out. A useful urinary and sexual stump can be obtained by inserting a No. 20 F. catheter to aid in separating the corpus spongiosum from the corpora cavernosa; the latter are transected 1.5 cm. above the level of the former, which is transected at the level of the skin incision. The catheter is left in place until the skin sutures are removed.

FRANK DORRANCE

Intrinsic Factors Altering the Absorption of Catgut. Kraissl, C. J., *Surg., Gyn. & Obst.*, 1936, **63**: 561.

Great variation was found in the length of time of digestion of strands of catgut of the same variety; most of the defects were found at the point where the strands were bent in the tube and because of the presence of foreign bodies of amorphous material. Non-boilable catgut absorbs less water, and it was found to resist digestion longer than the boilable or chromicized catgut. Chromic catgut of size 00 (medium-hard or 20-day variety), if well permeated during its processing, was found as resistant to digestion as the larger sizes in which permeation is less certain. Allergic individuals were found to be more prone to wound disruption. This was also true of those non-allergic persons who had had previous operations in which catgut was used as suture material. Allergic individuals may become sensitive to catgut and to chromic acid. The author was able to develop hypersensitivity to catgut and to chromic acid in guinea-pigs, and

found the majority of the wounds disrupted. In 56 cases of wound disruption in patients he found that 4 had history of allergy and 32 had had previous operations; he was able to make intradermal tests of 19, finding 4 sensitive to plain catgut, 10 to chromic catgut, and 10 to chromic acid.

FRANK DORRANCE

Femoral Hernia. Dickson, A. R., *Surg., Gyn. & Obst.*, 1936, **63**: 665.

The integrity of all hernial orifices is dependent upon fascial strength. In the region of the femoral canal the intimate connection of the fascia iliaca and the transversalis fascia is less strong than lateral or medial to it. Dickson recommends the Lotheissen technique (inguinal canal approach), as allowing a higher ligation of the hernial sac, and would incise the transversalis fascia parallel to the inguinal ligament, mobilize it until he was freely able to approximate it to the pectineal (Cooper's) ligament, and suture with three interrupted chromic catgut sutures. The most lateral suture was placed just medial to the femoral vein. The internal inguinal ring may be narrowed by suture. The spermatic cord was dropped back into place.

FRANK DORRANCE

Obstetrics and Gynæcology

Anæmia in Pregnancy. Adair, F. L., Dieckmann, W. J. and Grant, K., *Am. J. Obst. & Gyn.*, 1936, **32**: 560.

The means for the hæmoglobin concentration in pregnancy are 11.56 g. per 100 c.c. of blood; for the cell volume 37.31 volumes per cent; and for the erythrocyte count 3.77 million. The minimum standards for normal pregnancy are 10 g. of hæmoglobin per 100 c.c. of blood; 33 volumes per cent for the cell volume; and 3.36 million for the erythrocytes. Eleven and six-tenths per cent of our pregnant patients have an anæmia according to these standards, but if the standards for the non-pregnant patients are used 63 per cent must be classed as anæmic.

A normal decrease and increase in the hæmoglobin, cell volume and erthrocyte count occur during pregnancy. These changes cannot be altered by treatment. The fluctuation may amount to 2.3 or even 6.0 g. of hæmoglobin within a period of four to six weeks. Knowledge of these marked fluctuations should make one particularly cautious about attributing increase in the hæmoglobin concentration, cell volume, and erythrocyte count to any previous treatment.

An adequate amount of transfused blood will raise the hæmoglobin concentration to normal permanently and relieve all the symptoms and signs of anæmia. Blood transfusion during pregnancy, if done properly, has no deleterious effect on the mother or the fetus. It has not caused premature labour.

The prevention of the anæmia of pregnancy is easier than the cure. An adequate diet, with proper hygiene, is the best prophylaxis. A normal hæmoglobin content is essential for the normal functioning of the organs of the body. Toxæmia is less likely to occur, the patient is better able to tolerate blood loss and the strain of labour, her tissues have more resistance, she is less likely to become infected, and her recovery after delivery is more rapid.

ROSS MITCHELL

Spontaneous Rupture of the Membranes Before the Onset of Labour. Ballard, M. B., *Am. J. Obst. & Gyn.*, 1936, **32**: 445.

Four hundred and twenty-five cases of spontaneous rupture of the membranes before the onset of labour were analyzed as to parity, age, race, latent period, duration of labour, relation of baby's weight to the latent period, relation of baby's weight to duration of labour, relation of abnormal presentations to the latent period and duration of labour, methods of delivery, cause of rupture, complications, maternal morbidity and mortality, condition of babies at birth, and infant mortality during the first two weeks of life. The 425 represented approximately 7 per cent of the total deliveries in a six-year period on the obstetrical service of the University of Maryland School of Medicine. The average latent period for primigravidæ was 13.17 hours and for multigravidæ 21.41 hours. Parity apparently had no effect upon the frequency of rupture. The average duration of labour was less for all patients than that generally accepted as normal. There was no relation of the baby's weight to the latent period or to the duration of labour that could be demonstrated as due to the premature rupture of the membranes. There was no lengthening of the latent period or the duration of labour in the abnormal presentation group. Operative deliveries were not increased. Toxæmias, syphilis, and twin pregnancies appeared to cause rupture of the membranes before the onset of labour. Abnormal presentations might play some part. Complications were rare, the most frequent being infection.

The corrected morbidity was 0.025 per cent, the corrected maternal mortality was zero. Ninety-one decimal fifty-six per cent of the babies were born alive at full term. Only two dead babies could definitely be said to be the result of early rupture of the membranes, and none dying within the first two weeks of life could be attributed to this cause.

ROSS MITCHELL

Cæsarean Section in Dystocia. Hanna, G. C., *Am. J. Obst. & Gyn.*, 1936, **32**: 452.

In cases of dystocia which have been neglected and poorly managed two types of uteri may be distinguished. In one, the hand cannot be passed any distance into the uterine cavity because of obstruction from the contraction ring;

in the other, there seems to be an absence of uterine walls because of the great dilatation of the organ. In both types embryotomy of the dead fetus is not without danger to the mother because of the possibility of hæmorrhage, shock, rupture of the uterus and infection. In cases in which craniotomy is even more difficult and hazardous than usual Cæsarean section, with hysterectomy and drainage, offers the safest and best means of delivery. The necessity for the performance of this operation is rare. Improved obstetric teaching and supervision in medical schools and hospitals have resulted in more intelligent and careful practice. No problem presents greater need for good and careful judgment in its management than a dystocia which has been badly handled before consultation.

ROSS MITCHELL

Pædiatrics

The Presence of the Meningococcus in the Nasopharynx of Normal Individuals and the Bactericidal Property of Blood against the Meningococcus. Silverthorne, N., *J. Pædiat.*, 1936, **9**: 328.

Studies of the carrier rate of contact and non-contact persons during and between epidemics of meningococcic meningitis have been made by a number of investigators, and vary from quite low figures to as high as 60 per cent in one naval and military non-contact population.

The present work consists of a report of the results from 1,227 throat cultures taken monthly over a two-year period from 63 normal healthy persons, mainly physicians and technicians. No less than 243 cultures (19.8 per cent) were positive for the meningococcus. The monthly percentage varied from 16 to 28. Of 26 persons who at one time or other had a positive culture, 11 showed the organism fairly persistently, 13 intermittently, and 2 on only one occasion.

Of the 11 carrier strains found, 3 were shown to be virulent and 8 avirulent, on a basis of the mouse—mucin and bactericidal tests. At least some of the carriers possessed in their blood bactericidal properties against their own and other virulent strains.

ALAN ROSS

Radiology and Physiotherapy

A Factor of Importance in Radio-sensitivity of Tumours. Mottram, J. C., *Brit. J. Radiol.*, 1936, **9**: 606.

Cells forming the margins of carcinomatous masses are more sensitive to gamma radiation than are central cells, because the marginal cells are nearer the blood vessels and therefore are better supplied with oxygen. The central cells are nearly anaerobic and so more radio-resistant. It follows that small cell masses of carcinoma should be more radio-sensitive. Radiation dosage should be so spaced as to catch the tumour in a radio-sensitive stage and withheld during stage of radio-resistance. The period of growth corresponds with sensitivity and regression with resistance.

A. S. KIRKLAND

Roentgenological Consideration of Lymphoblastomata. Roentgen Pulmonary Pathology of the Hodgkins' Type. Pierce, C. B., Jacox, H. W. and Hildreth, R. C., *Am. J. Roentgenol.*, 1936, **36**: 145.

From 681 cases seen in ten years, 214 cases with intrathoracic disease of the Hodgkin's type or sarcomatous Hodgkin's type of lymphoblastomata were studied exhaustively. The clinical symptoms or signs and the blood changes often suggest this disease, but are not indicative of the extent of chest involvement. The x-ray evidence of adenopathy or parenchymal infiltration is commonly far greater than the clinical signs or symptoms would suggest. There is nothing pathognomonic of this disease in the x-ray examinations, as all common changes may be found. The x-ray appearance is not of value in prognosis. At least one-third of this series presented normal chests on roentgenological examination, but in the other two-thirds the x-ray examination offered the best opportunity, short of pathological study, for the diagnosis of the disease and the estimation of its extent.

A. S. KIRKLAND

Roentgen Therapy of Hodgkins' Disease. Pierce, C. B., Jacox, H. W. and Hildreth, R. C., *Am. J. Roentgenol.*, 1936, **36**: 165.

Of 315 patients with this disease observed, roughly half received roentgen treatment. Half of those treated received repeated local irradiation; the other half received irradiation over the entire lymphatic system. No unfavourable biological changes were observed following either method of irradiation, and a definite extension of life resulted following irradiation by either method. Either method is equally effectual in prolongation of the total duration of disease from present figures, but more favourable figures may be expected from that group of patients now under observation who have received systemic irradiation, and the authors feel that systemic irradiation of all lymphoid areas is the method of choice in the light of symptomatic response.

A. S. KIRKLAND

Roentgenological Observations on Various Types of Chronic Arthritis. Taylor, G. D., Ferguson, A. B., Kasbach, H. and Dawson, M. H., *Arch. Int. Med.*, 1936, **57**: 979.

This excellent article is in the nature of a preliminary report of 300 cases observed in detail and grouped clinically as follows:—(1) rheumatoid arthritis, (2) osteo-arthritis, (3) gout, (4) gonococcic arthritis, (5) tuberculous

arthritis, (6) rheumatoid spondylitis, (7) Still's disease. In each of these groups the roentgenological findings were described, analyzed and charted under 15 chief items, with 49 detailed descriptive roentgenological subdivisions. Six of the more outstanding items: (1) decalcification, (2) production of bone, (3) destruction of bone, (4) joint space, (5) ankylosis, (6) change in soft tissue are described and defined. In addition charts were prepared showing the percentages of "items" observed in each clinical group. As an aid in differential diagnosis these charts show a combination which is characteristic for each of the seven types. Rheumatoid arthritis and osteo-arthritis were shown to be distinct entities. "Roentgenograms, properly interpreted, are a valuable aid in the differential diagnosis and prognosis of the various types of chronic arthritis."

HILL H. CHENEY

Therapeutics

Blood Regeneration in Patients with Hæmatemesis of Melæna from Peptic Ulcer, Treated with the usual Ulcer Cure and with the Meulengracht. Schiodt, F., *Am. J. M. Sc.*, 1936, **192**: 163.

Schiodt compares the results obtained by treating 10 patients with hæmatemesis from peptic ulcer by means of a purée diet and iron with an equal number on the usual ulcer cure. The purée diet was introduced by Meulengracht in 1931, and includes meat, fish, vegetables, fruit and jellies. The iron administered was lactate of iron in 50 centigram doses thrice daily. This was combined with sufficient cascara to counteract any constipating effect. The patients on this high iron diet were subjectively and objectively better than those on the usual ulcer cure. Further, hæmoglobin regeneration was much more pronounced. The average hæmoglobin on admission of the 10 patients on the usual cure was 47.5 per cent. Twenty days later it was only 50 per cent. The average hæmoglobin of the 10 patients on the Meulengracht diet was, on admission, 50 per cent. Twenty days later it was 68.4 per cent. The author feels that proper food alone is of definite value for the regeneration of blood, whether or not the effect is supported by the giving of iron.

E. S. MILLS

Experiments with "Depepsinized" Human Gastric Juice in the Treatment of Pernicious Anæmia. Fitz-Hugh, T., Jr. and Creskoff, A. J., *Am. J. M. Sc.*, 1936, **192**: 168.

Three patients suffering from pernicious anæmia in a state of relapse were given intramuscular injections of "depepsinized" concentrates of fasting gastric juice obtained from the patients themselves. This treatment was ineffective in producing a reticulocyte response indicative of a remission of the disease. A fourth patient in the same state was given orally "depepsinized" fasting gastric juice obtained from a normal individual. As in the first experiment no significant reticulocyte response resulted. In the third set of experiments two patients in the relapse phase of pernicious anæmia were given intramuscular injections of "depepsinized" gastric juice from normal subjects. Again no significant reticulocyte response followed. The results of these experiments, therefore, fail to substantiate the claims of Morris and his co-workers and of Greenspon as regards the sole importance of the intrinsic factor in gastric juice. They would tend to strengthen Castle's original conception that the intrinsic factor alone is inadequate to produce a remission in pernicious anæmia, but that its interaction with protein is essential.

E. S. MILLS

The Corbus-Ferry Gonococcus Filtrate. Deakin, R., *J. Am. M. Ass.*, 1936, **107**: 954.

The author reports the results of a study of Corbus-Ferry filtrate conducted by the outpatient department of the genito-urinary section of the Washington University. The report consists of the results obtained in 52 cases treated with the filtrate and 30 control cases. The local treatment was the same in both groups and consisted of urethral injections of 0.5 per cent strong silver protein twice daily and santal oil by mouth. The filtrate group received in addition weekly intradermal injections, starting with 0.5 c.c. and increasing to 0.7 c.c.

They found that 73 per cent of the patients who received only local treatment got a satisfactory clinical result, whereas only 46 per cent of those who received filtrate in addition to local therapy did so. Further analysis showed that it was the acute cases on the filtrate which suffered most by comparison with the acute cases in which it was not used. Even in chronic gonorrhœa the percentage of satisfactory results was greater in the group not receiving the filtrate. The poorest results with the filtrate were obtained in the cases of chronic gonorrhœa with a positive complement fixation test, and the best results in cases with a negative test, but even at that the results in this group were not superior to those in patients who received no filtrate.

N. E. BERRY

Pathology and Experimental Medicine

The Relationship between Alcoholic Intoxication and Anoxæmia. McFarland, R. A. and Barach, A. L.: *Am. J. M. Sc.*, 1936, **192**: 186.

The authors have studied the behaviour of 23 subjects in an oxygen chamber under various degrees of alcoholic intoxication. The atmosphere of the oxygen chamber contained 50 per cent oxygen and from 0.2 to 10 per cent carbon dioxide. The drinks varied from 0.75 to 1.25 grams of ethyl alcohol per kilo of body weight,

diluted to a total volume of 250 c.c. with water and orange juice. The efficacy of the excess oxygen and carbon dioxide in counteracting the effect of the alcohol was determined by analyzing samples of venous blood for blood alcohol and lactic acid. Alterations in behaviour were studied by a series of six psychological tests. The respiration, pulse and blood pressure were taken at regular intervals. The experiments were suitably controlled in atmospheres of air and low oxygen with and without alcohol. The results were as follows:—The amount of alcohol in the venous blood showed a tendency to decrease while breathing 50 per cent oxygen and excess carbon dioxide as compared with air. The increase in blood lactic acid after ingestion of alcohol in ordinary air was not present when the patients were tested in the O_2 and CO_2 atmosphere. The differences in both these observations amounted to as much as 50 per cent. Pulse and blood pressure fluctuations were not nearly so marked in the CO_2 and O_2 atmosphere as in ordinary air. There was also a general tendency toward improvement in the six psychological tests (Code, Dotting, Colour-naming and Pursuit Meter tests) when conducted with the patients in the oxygen-carbon dioxide atmosphere. The authors, therefore, conclude that patients suffering from alcoholic intoxication show improved mental and motor behaviour in an atmosphere of CO_2 and O_2 as compared with ordinary air. There was no evidence to show whether this improvement was due to differences in basal metabolism, general physiological condition or physiological idiosyncrasies in the rate of oxidation.

E. S. MILLS

Hæmophilia. I. The Abnormal Coagulation of the Blood and its Relation to the Blood Platelets. Patek, A. J., Jr. and Stetson, R. P., *J. Clin. Investigation,* 1936, **15**: 531.

The one abnormality constantly found in hæmophilia is the inability of the blood to coagulate in a normal manner. This defect is demonstrable usually by a prolonged clotting-time, which in turn determines the various manifestations of the disease. Further understanding of this malady depends, therefore, upon knowledge of the prolonged clotting-time. Most investigations of the blood-clotting mechanism in hæmophilia have been made with methods involving the recalcification of oxalated or citrated plasma, and have been interpreted in terms of the several theories of blood coagulation. In the present study this approach was abandoned, for two reasons. (1) The recalcification of plasma is an artificial indirect procedure which may not reflect physiological changes; and (2) the theories of blood coagulation, with their varied nomenclature, possibly have served to confound rather than clarify the understanding of the disease. The study here is based upon the well-recognized observation that transfusion with normal blood reduces the clotting-time of whole blood in cases of hæmophilia. It was assumed, therefore, that normal blood contains a substance which either supplies a clotting factor which is lacking in hæmophiliac blood or which counteracts a mechanism inhibiting coagulation of the blood in hæmophilia. An analysis of the nature of this substance or substances was the aim in this investigation. This enquiry has, of course, been made by other workers, but their methods and concepts differ from those of our authors. The latter found that the addition of platelets to hæmophiliac blood did not shorten the clotting time, whereas the addition of a minute quantity of platelet-free normal plasma abruptly reduced the clotting-time, indicating that the platelets were not involved in the clotting abnormality of hæmophilia, and that the defect resided in the plasma. Studies *in vivo* with filtered normal plasma supported this contention. This does not imply that platelets are unimportant in coagulation, but they inferred from their study that the platelets in cases of hæmophilia function as well as they do in normal persons. Further studies are being made by the authors to identify the effective substance contained in normal plasma

JOHN NICHOLLS

Cholesterol Content of Blood in Diabetic Patients Fed Diets Rich in Fat. Freyberg, R. H., Newburgh, L. A. and Murrill, W. A., *Arch. Int. Med.,* 1936, **58**: 589.

The authors deal with the question as to whether increased blood cholesterol is a result of high fat diets or has any relation to food intake, and whether atherosclerosis is related to blood cholesterol increase. Many authorities are sure that a high fat diet produces a high blood cholesterol. The investigation reported was made on 21 patients in the Ann Arbor University Hospital, who were all receiving high fat diets but were under good control regards their diabetes. Allowing considerable range in what is considered a normal blood cholesterol, all the cases gave normal readings, and whatever variation was present was in no way related to the amount of fat in the diet. Secondly, as far as their animal experiments were concerned, the development of atherosclerosis was in no way related to the height of the blood cholesterol. There is a great division of opinion among authorities in this matter, with the experimental results contradicting each other. The authors suggest that some of the confusion is because all the cases are not under good control, without which estimations of blood cholesterol would all tend to reveal high readings.

P. M. MACDONNELL

Obituaries

Dr. Vaughan Elderkin Black, of Moose Jaw. A few weeks ago one of the most widely known and best loved of McGill graduates, Dr. Vaughan Black, was struck down by a motor car, sustaining injuries from which he died a week later, on September 14th. During that anxious week only slight hope was held for anything but a fatal termination.

The sad news that Vaughan Black had been so suddenly taken away caused McGill men everywhere a feeling of deep personal loss. It is given to only a few to achieve what he did in so many different spheres. Perhaps, if he himself could evaluate his own accomplishments he would rate his capacity to make and enjoy enduring friendships—his power to win respect and love of so many of his fellowmen—as the thing which gave him greatest joy of life. Surely few men have inspired, as did he, the admiration and affection of so many of his fellows.

Vaughan Black was born at Amherst, N.S., in 1884, the only child of Dr. Allan and Elizabeth Black. His father, a highly respected medical man, also died in his early fifties. His mother predeceased him a number of years ago. In 1917 he married Miss Nell Elderkin, also a native of Nova Scotia. There are three surviving children, Miss Barbara, the eldest, Elizabeth, and Allan. The first-born, a son bearing his father's name, died in early childhood.

After leaving high school, Vaughan Black entered the Arts class of 1906 at Mt. Allison, Sackville, N.B. Because of his athletic prowess he naturally was prominent in college life throughout his course. The kind of hero-worship which surrounds a great athlete in a small college is likely to turn the heads of many,—but not so with Vaughan. Modest and unassuming, he took athletic honours in his stride, but never forgot his main object in taking the Arts course—to prepare himself for his medical course, and his life's work.

He went up to McGill in 1906 and graduated in 1910, taking a post-graduate year at the Montreal General Hospital. Scarcely had he arrived in Montreal when he was in demand for Rugby and track sports, and later he distinguished himself in both, and was Captain of the McGill Rugby team in his third year. Many will remember his playing. Powerful, extremely fast for a man of his weight, and with a deadly "straight arm", he was sensational on the Rugby field. He could give and take hard knocks with the best, but was always the truest sportsman and gentleman. Academically, his standing throughout his medical course was universally high. A good reliable student, he was no book-worm, finding time for those contacts and companionships of college life which so often lay the foundations of future years of friendship. After an intern year at the General Hospital, Montreal, he turned to the Canadian West, then in the stage of rapid growth and development, coming to the city of Moose Jaw. There he established his practice, set up his home, and raised his family, and there he died, after twenty-four years, leaving behind him a memory of professional and community service that will be cherished in that city for many years to come.

In 1912 he associated himself with Dr. T. M. Leask, well-known western surgeon and war-time medical officer, and they remained together through twenty-three years. Later, Drs. Burwell, Young, and Parkins were added to the firm. The words of Dr. Leask, greatly mourning the loss of his friend and colleague, are significant:—"Vaughan and I were together for twenty-three years, and never a harsh word passed between us".

To outline in any adequate way the life of Dr. Vaughan Black as a medical man and as an outstanding citizen of his community during the twenty-four years he was given to live in Moose Jaw is perhaps outside the scope of this review. He possessed all the attributes of a good doctor—skill and ability, undoubtedly, fine judgment, a great fund of good common sense, and a kindliness inherent and ever present. With patients he was friendly, but frank and firm when the occasion demanded. He had great sympathy and understanding for the poor or unfortunate person, and in all his dealings proved himself worthy of his chosen calling.

He was a good disciple of Osler in that he regularly attended medical meetings. He frequently addressed both local and provincial Societies, and was a Past-President of the Saskatchewan Medical Association. In medical circles in Saskatchewan his influence will be sorely missed. His opinions were listened to and were usually sound. In a quiet, yet impressive, way he was often able to resolve difficulties and to smooth the way for the accomplishment of the purposes desired.

Beside his Arts and Medical degrees, he also held the F.R.C.S.(C.), and the F.A.C.S. Only this year he was honoured by the Canadian Medical Association by being appointed Chairman of the Osler Memorial Fund. This year also he had just been appointed by the Saskatchewan Government to the new Health Services Board, representing the Medical Profession of Saskatchewan as one of the three members of the Board. He did not neglect post-graduate study, and on two occasions, 1924 and 1929, he studied in Europe, taking up chiefly surgical work.

As a loyal and public-spirited citizen of Moose Jaw, Dr. Vaughan Black was outstanding through all his years. Pages would be required to tell of his fine contribution to the life of that city. He was constantly in demand to assist in some enterprise—if not to take the lead—and he sacrificed himself freely. He gave generously in time and money for the support of all worth-while movements, particularly those of a cultural and charitable nature, for the welfare of the city and its people. That such a man should so suddenly be removed from the life of service which he loved—from a home and family to which he was most sincerely and deeply devoted—seems indeed a cruel misfortune. The comforting thought is that his example and influence will linger on. A gentleman, a good sportsman, a credit to his profession, a loyal friend, he will not be forgotten.

W.A.D.

Dr. Edmond Stanislaus Aubry, of Hull, Que., died at his home October 20, 1936, after an illness of several months. He was 76 years old.

He was a native of Ste. Scholastique, Que., graduated from Victoria University, Montreal, in 1882, and the same year started his practice in Hull. Actively interested in civic affairs, he was alderman from 1888 until 1893, when he was elected mayor, and held the latter office until 1899. He was re-elected mayor in 1905 and 1906.

Dr. Robert Wilfred Moss Clark, of Niagara Falls, Ont., died on October 25, 1936, aged 32 years. He was a graduate of Queen's University (1934).

Dr. John Scoular Goodfellow, of Morrisburg, Ont., died in October, 1936. He was born in 1871, and a graduate of the Medical Faculty of Trinity University (1894).

Dr. Joseph Garceau, the first doctor to take up practice in Shawinigan Falls, Que., died in hospital on November 8, 1936. He was 65 years of age.

A native of Louiseville, Dr. Garceau studied at Three Rivers Seminary and took his degree in medicine at Laval Medical School, Montreal (1899).

Dr. Melbourne Franklyn Keith died in Moncton on October 11, 1936, Dr. Keith studied medicine at the University of Toronto and graduated in New York University (1882). The late Dr. Keith was born in Havelock, the only son of the late Owen and Sarah

Keith, and was a great-grandson of the late Daniel Keith, one of the United Empire Loyalist pioneers in that place. Receiving his early education in Havelock, he was a school teacher for a few years. After receiving his medical degree he began to practise his profession in Harcourt, and continued to practise until 1906, at which time he retired. He has lived in Moncton since his retirement.

Dr. John McDiarmid, who was associated with the life of Brandon from its inception and was mayor of the city for five years, died on October 16th, in his ninety-first year. When he arrived fifty-four years ago he was the only physician in the town, then only a pioneer settlement. He carried on practice until 1914, when he retired, but retirement brought no slackening in his community interest. He was a member of the Session of St. Paul's United Church and Past-Master of the Masonic Lodge.

Dr. McDiarmid was born in Fingal, Ont., and graduated in medicine from Trinity College, Toronto (1874). He practised for a time in Brainstone, and came to Brandon in 1882.

Dr. Peter McGibbon, of Bracebridge, Ont., died on October 10, 1936, after a lengthy illness. Dr. McGibbon was the son of the late Donald McGibbon and Isobel Cameron, Arkona, Lambton County, being of Scottish extraction and was a graduate of the University of Toronto (1904). He was L.R.C.P. and M.R.C.S. (1916).

Although not in good health, Dr. McGibbon had been able, with assistants, to look after his extensive practice in Bracebridge and throughout the Muskoka District, as well as attend to his Parliamentary duties until his defeat in the Dominion elections in 1935. He first sat for the constituency of Muskoka-Ontario following his victory in the 1917 general elections. He was defeated at the polls in 1921, but was re-elected at general elections in 1925, 1926, and 1930. Dr. McGibbon was a Conservative in politics. During his career in the House of Commons he was noted for his interest in the administration of the Canadian National Railways. At one time he was a member of the Committee on Pensions and Re-establishment. He was fitted for work on the committee because of his war service. During his term overseas he was Medical Officer for the 8th Royal Berkshire Regiment and the 1st Black Watch. "For conspicuous gallantry" he won the Military Cross at the Battle of Loos, October 13, 1915. He led a party of stretcher-bearers between the lines and at great personal risk succeeded in rescuing many wounded men. At his death he held the rank of Lieut.-Colonel.

Dr. Joseph Henry Radford, of Galt, Ont., died on November 8, 1936. He probably held a record for municipal service in Canada, serving for 53 consecutive years. He had held every municipal office within the gift of the electors.

Dr. Radford was born on February 12, 1857, on a farm at Bathurst, Lanark County, near Perth. He attended a country school, later Perth Collegiate, and for four years taught at Bathurst. He then went to the University of Toronto and took a medical course, coming to Galt on July 4, 1880, to practise. Two years after his arrival here, he married the daughter of Dr. John R. Philip, of Galt, who predeceased him.

Dr. Radford was a past-president of the Ontario Medical Health Officers' Association.

Dr. Herbert Lionel Reddy, of Montreal, died on November 4, 1936, at the age of 82. Born in Montreal in 1854 young Reddy was taken to Ireland—the ancestral home—and secured his first education at the Portaro Royal School at Enniskillen on Loch Erne. Returning to Canada at 17 young Reddy entered McGill, graduating in arts in 1873 and in medicine in 1876.

Following graduation Dr. Reddy went to England. There he entered St. Thomas Hospital, London, serving his internship, and later going to Vienna for a post-graduate course, where he spent a year. Returning to Montreal, he became professor of obstetrics at Bishop's College for a time before assuming the post of physician in charge of the Women's Hospital, then situated over the old Western Hospital. That was in 1886, four years before nursing as a profession got well under way in Canada, and it was the beginning of an uphill fight for the better treatment and care of women patients, a fight which was to continue for fifty years without fear or favour so long as his patients reaped a benefit.

The Women's General was started in 1870 when Bishops University decided to have a medical faculty in Montreal. It was not until 1886 that Dr. Reddy took charge, the hospital quarters at that time being on the top floor of the old Western Hospital. When it was announced that the Western was going in for general work the Women's had to move down to Osborne Street and was twice forced to vacate rented premises through the expansion of the Canadian Pacific Railway terminal at Windsor Street.

For some years the work was carried on in a group of houses on St. Catherine Street, a short distance east of Western Square at Atwater Avenue. In 1926 it was decided to move to a building of their own to be built, the present site on Tupper Street having been decided upon. There Dr. Reddy had a building and equipment much more to his liking. With a five-storey edifice and 250 beds the work has gone forward, Dr. Reddy not only being the chief physician but superintendent and business manager as well. He was credited with having conserved the resources of the institution in such a manner as to place it on a sound basis financially. He lived to see that worthy work housed in a modern structure with splendid equipment and to observe the fiftieth anniversary of his connection before he died.

Besides his McGill and Bishop's College medical degrees, he received the diplomas of L.S.A. (London), L.R.C.S. (Edinburgh), and L.R.C.P. (London).

Dr. Reddy's death terminates a unique record in medical history as well as of devotion to a humane ideal. His work for the alleviation of suffering womanhood and its association with the work undertaken by the Women's General Hospital, of which he was the chief builder and presiding genius will entitle his name to a place on the roll of medical science achievement.

Dr. Robert C. West, of Woodstock, Ont., died there on October 17, 1936. He was born nearly 84 years ago in Darlington Township, near Oshawa, Dr. West was a graduate of Trinity Medical College, Toronto (1886), and later studied at the University of Edinburgh. He retired in 1933.

Be substantially great in thy self, and more than thou appearest to others; and let the World be deceived in thee, as they are in the Lights of Heaven. Hang early plummets upon the heels of Pride, and let Ambition have but an Epicycle and narrow circuit in thee. Measure not thyself by thy morning shadow but by the extent of thy grave, and Reckon thyself above the Earth by the line thou must be contented with under it.—Sir Thomas Browne.

Happy is the man who has been able to learn the causes of created things, and has put under his feet all fears and unyielding fate, and has heeded not the noise of Death's devouring stream.—Virgil.

News Items

Great Britain

Research workers in Great Britain, and indeed most medical men, are agog with interest and excitement over the announcement that Lord Nuffield (formerly Mr. W. R. Morris) of motor car fame has donated £1,250,000 to Oxford University for purposes of medical research. More than eight years ago Mr. Morris (as he then was) began to show his interest in medical matters. He built a new maternity home for the Radcliffe Infirmary. He bought the site of the Radcliffe Observatory, which institution was transferred to South Africa. He enlarged and modernized the Infirmary, and a little later equipped the Institute of Medical Research, which has been in operation for rather more than a year. The latest gift is the largest ever made by one individual in the country.

Sir Farquhar Buzzard, Regius Professor of Medicine at Oxford, in his presidential address before the British Medical Association last July, stated that he had an "ambitious dream" that Oxford should be the home of a school for research in which men and women, freed from the burden of practice and of routine teaching, should give their lives to research and train others to do the same. Lord Nuffield seized the psychological moment, and Sir Farquhar's dream is to come true. Not less noteworthy than the gift itself is the statesmanlike plan on which the school is to be developed. Lord Nuffield's declared purpose is to advance medical science by enabling his University to take the lead in research and the hospitals of his native city to cooperate in making Oxford the greatest of medical research centres. He also has expressed the hope that the new research institute will turn out about twenty brilliant men in a year and that these will go to other centres to carry on the work of teaching.

Lord Nuffield had already given, it is said, more than one million pounds to hospitals and other causes. The Radcliffe Infirmary has received from him the sum of £140,000; the Wingfield-Morris Orthopædic Hospital, £70,000; and St. Peter's Hall, £72,000. Guy's Hospital, of which he is the treasurer, has received £65,000, and on the morrow of the announcement of the Oxford gift it was stated that Lord Nuffield had made himself responsible for £80,000 more in connection with that hospital's appeal for funds to extend the nurses' home. St. Thomas's Hospital has received from him a total of £104,000 and the new Birmingham Hospital Centre, £52,000. His recent series of gifts includes £5,000 a year for seven years for the development of books for the blind. As evidencing his interest in fields of usefulness other than those strictly medical and scientific, Lord Nuffield, in the letter offering his gift of one million and a quarter pounds for the Research Institute, added the welcome postscript that he wished to give an additional £100,000 for the benefit of the Bodleian Library and other projects. A day or two later came a gift of £30,000 for the Acland Nursing Home in Oxford. These are princely benefactions and will do much to facilitate the work of research medicine, and thereby add to the well-being of many thousands, not only in Oxford but in Great Britain, and, indeed, throughout the whole world.

Alberta

The Honourable Dr. William Egbert, a former Lieutenant-Governor of the Province of Alberta, and for many years a member of our profession in Calgary, died after a long illness on October 15th, 1936.

The College of Physicians and Surgeons is issuing a copy of the Alberta Register, the first complete one since 1924. During the decade over 180 registrants have passed away; only 85 were actually in residence in Alberta at the time. From 1925 to 1936, one hundred and twenty medical graduates of the University of Alberta registered in this province. Of these 37 registered elsewhere and have left; 2 are deceased; and the remainder, 81 in number, are still practising here.

The College of Physicians and Surgeons is holding elections in three districts this year, *viz.*, Lethbridge, Camrose and Calgary Districts. The term is for two years, with no limit to the number of years a representative may serve. There are seven districts in all, and last year four men were elected.

Recently Alberta lost one of its best qualified men, Dr. Emerson Smith, Edmonton, Professor of Urology in the University of Alberta, who moved to the City of Ottawa.

It is reported that Edmonton is considering paying the medical men of that city the sum of $20.00 per month in slight recognition of their services to people on relief. This is a similar arrangement to what is in existence in Calgary. When one considers in Calgary this represents about thirty-three cents per call, which provides nothing for operations, which average seven per day, it makes one wonder why the people feel the profession should carry such a burden when no other class of citizens is called upon to act similarly.

Gradually contract practice is increasing, partly owing to the drought and the depression, and partly owing to the desire for assurance that medical attention may be bought at wholesale rates. One notices however that there is ever a desire to get more for the patients and give less to the physician. The fact that a physician has established himself in the town, has rendered good services, and has built a house, indicating permanency, weighs little when the saving of dollars at the expense of experience is in the balance.

Since the early fall of 1935 there has been a steady increase in the number of cases of a mild type of scarlet fever in the City of Calgary. Even during the past summer this disease continued to appear. During the present fall it has assumed epidemic proportions. The Isolation Hospital has been filled to capacity, and there does not seem at this date to be any marked subsidence of the disease. During the past twelve months there have been close to 800 in this City.

G. E. LEARMONTH.

British Columbia

It has been decided by the Board of the Vancouver General Hospital to request the Vancouver City Council to submit at the next civic elections a by-law for the construction of a new nurses' home, costing about $1,000,000. It is proposed to erect a building of approximately 500 rooms. At the present time the quarters for accommodation of the nurses of the General Hospital is greatly overcrowded, some rooms having as many as three occupants, and no nurse has a room to herself.

A bequest in the will of Wm. Richardson Hall of West Lorne, Ontario, who died on September 3rd, 1935, provided for a legacy of $1,500 to "the consumptive sanatorium, Grangeville, B.C.". Mr. Justice Henderson, of Ontario, recently, in deciding as to the disposition of this bequest, noted that there is no such place as Grangeville in B.C., and ruled the money should be paid to the Province of British Columbia for the benefit of the Tranquille Sanatorium.

Dr. A. B. Schinbein, of Vancouver, has been elected second vice-president of the American College of Surgeons in the convention recently held in Philadelphia. He assumes his new position in 1937.

It is stated that the hospitals of B.C. may have to face a revision of their government grants as a result of the inauguration of health insurance, which the government believes will alter the financial position of many hospitals, since large numbers of patients who could not pay in the past will pay in future through the Health Insurance Plan.

WHEN WINTER WINDS BLOW

January-February blizzards are "just around the corner", waiting to catch the unwary, those unfortunates whose low resistance to respiratory infections constitute a never-ending problem for the physician. Clinical experience does give us, however, sound reason to believe that vitamin A and D therapy builds up a definite resistance to the inroads of infection of the epithelial tract.

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ALPHAMETTES

Misleading headlines continue to appear in the *Vancouver Daily Province* concerning Health Insurance. A column in the issue of October 24th is headed "B.C. Insurance plan endorsed", but the gist of the half-column that follows is that employers and employees are turning in the health insurance registration forms in large numbers, which they are legally required to do. Neglect to do so is punishable by penalities.

The Metropolitan Health Board Committee held its first meeting in the City Hall on October 22nd, and, after making tentative organization arrangements, decided to recommend to the City Council the appointment of three directors for the board health units. Those named are Dr. R. Brandon, of the Connaught Laboratories, Toronto, and Drs. A. R. Boyd and A. M. Menzies, of Vancouver, B.C.

Dr. J. Douglas Galbraith, who has been physician on the United Church mission boat, the *Thomas Crosby*, has been appointed medical superintendent of the Bella Coola General Hospital, taking over his new duties a few days ago.

D. E. H. CLEVELAND.

Manitoba

The Canadian Society of Clinical Surgeons met in Winnipeg on October 5th and 6th. Their meetings, held in the Board Room of the Winnipeg General Hospital, were open to the profession of Winnipeg and were most interesting.

The arrival of cold weather apparently has checked the epidemic of infantile paralysis which has prevailed for over three months. The largest number of cases occurred in rural Manitoba. The supply of convalescent serum has been adequate, and the mortality has been low in proportion to the number of cases. The reports indicate that serum when given in the pre-paralytic stage has been almost uniformly successful in preventing paralysis. The Provincial Government has announced its intention to provide the services of an orthopædic surgeon for the benefit of the children who have been left crippled.

At the invitation of the United Farmers of Manitoba and the United Farm Women of Manitoba Dr. C. R. Rice, of Winnipeg, addressed these bodies at their annual meeting held in Neepawa on October 27th. Dr. Rice appeared as a representative of the College of Physicians and Surgeons of Manitoba.

Dr. F. W. Jackson, Deputy Minister of Health in Manitoba, addressed the Dominion Public Health Association at Ottawa, and also gave a lecture to the Department of Public Health group of the University of Toronto on "Anterior Poliomylitis in Manitoba".

At the Memorial Day service held at the Medical College on November 11th, Mr. Robert S. Swan, President of the Medical Students' Association, placed a wreath before the tablet on which is engraved the names of the students of the College who have fallen in the Empire's wars, and Dr. John M. MacEachern, himself a combatant in the Great War, delivered an address.

Mr. John A. Forlong has donated $25,000 to the Winnipeg General Hospital, to be used in providing new x-ray equipment, especially for deep therapy, in memory of his wife.

ROSS MITCHELL.

New Brunswick

Dr. Robert Gregory, Assistant Superintendent of the Provincial Hospital, Saint John, has returned following some months' special study in mental hospitals in Great Britain.

Dr. G. A. B. Addy, of Saint John, has been re-elected a regent of the American College of Surgeons, his term to expire in 1939.

Dr. G. Clowes VanWart was the recipient of a presentation from the Fredericton Chapter of the New Brunswick Association of Registered Nurses at the end of a lecture presented to this Association recently. Dr. VanWart has lectured continuously for over forty years to the nurses in the Training School of the Victoria Public Hospital, Fredericton, and his gratuitous work in this connection has been very much appreciated. This is only another evidence of Dr. VanWart's many-sided activities in medical affairs in New Brunswick.

The first meeting of the fall session of the Saint John Medical Society was addressed by Dr. A. S. Kirkland, Radiologist for the Saint John General Hospital. His paper was "A review of successes and failures in x-ray therapy, covering the last fourteen years".

Early in October Dr. G. A. B. Addy visited Moncton where he consulted with the local hospital group *re* necessary steps for the formation of a Cancer Clinic. The meeting was largely attended and the local group will elect officers shortly.

It is announced in the press that the scheme of group hospitalization which has been under study for some months by St. Joseph's Hospital and the Saint John General Hospital in Saint John has almost reached the stage where operations may be commenced. The tentative date set for the enrolment of members will be probably at the beginning of 1937. Dr. S. R. D. Hewitt, Superintendent of the General Hospital, has been the moving spirit in this new departure in Saint John.

Dr. Richard Monahan, of the Provincial Health Staff, is at present in Toronto studying for his diploma in public health.

The meeting of the American College of Surgeons at Philadelphia attracted a very large delegation from all centres in New Brunswick.

A. STANLEY KIRKLAND.

Nova Scotia

At the opening meeting of the Hospital Standardization Conference in Philadelphia on October 19th twenty-one Nova Scotia Hospitals were approved, seven provisionally; fourteen were given grade A rating. The Tuberculosis Hospital in Halifax which has been functioning for sixteen years, and which was visited for the first time this year, is one of the institutions receiving approval.

Dr. A. F. Macaulay, Assistant Director of Medical Services and National Health, visited Halifax, where he remained for some days. During his stay he inspected Camp Hill Hospital. From Halifax he proceeded westward on his annual tour of inspection of Canadian Government Hospitals. The tour is expected to last two months.

Dr. Harry Stafford Morton, F.R.C.S. (Eng.), at present on the staff of the London Hospital, London, has been admitted to the Fellowship of the Canadian College of Surgeons.

The report of the survey on tuberculosis in Glace Bay district, carried out by Doctors Grant and Maclean of Dalhousie University, has been issued. The most important recommendations are the following:—that a full-time Health Department be established in Cape Breton, under a physician who has had special training, especially in tuberculosis; that this appointment be made by the Provincial Department of Health and that the chief duty of the Health Officer be the administration of the unit in Cape Breton, the supervision of annexes, and the conduction of the clinics. Further suggestions are:—the appointment of an Assistant Health Officer, three public

Earlier Discovery of Carcinoma

STATISTICAL data indicate that more than 40% of all carcinomas occur in the stomach. In the early stages, the disease presents no decisive physical symptoms. Hence, diagnosis often does not take place until the condition is far advanced . . . until it is too late for the most effective therapeutic measure—partial or total gastrectomy.

Earlier discovery of gastric cancer rests virtually upon x-ray examination before there are definite physical signs. In the majority of cases, radiographs will disclose most lesions in their incipient stages . . . Differentiation between benign and malignant growths also can be made. Treatment can be instituted when chance of successful results is favorable.

Don't delay examination of the patient by a competent radiologist in every case of obscure digestive disorder. The saving of long suffering . . . even life . . . may depend upon expeditious employment of this positive diagnostic measure.

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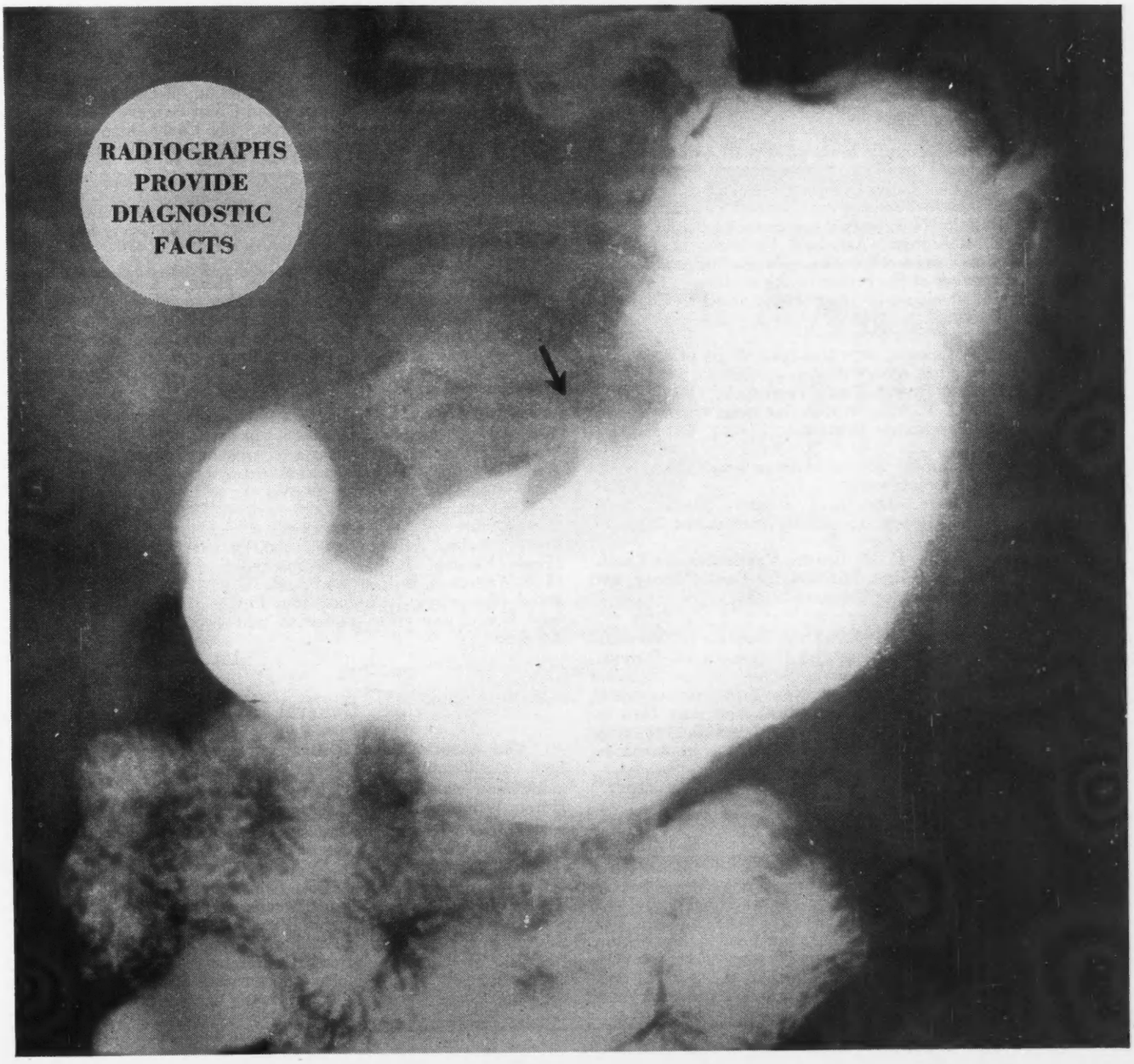

health nurses, devoting their whole time to tuberculosis control, and three public health nurses doing work of a general nature, such as, control of communicable diseases and maternal and infant welfare. Appointments of a social welfare worker and a dental surgeon are also included.

This report has been submitted to the Provincial Department of Health. The Minister, Dr. F. R. Davis, stated that measures are already being considered for establishing a public health unit in Cape Breton, and that it would probably be in operation during 1937. The United Mine Workers, in session at Truro, also discussed the tuberculosis situation in Cape Breton, and passed a resolution favouring the establishment of a Sanatorium modelled on the one at Kentville in preference to tuberculosis annexes.

Dr. W. R. Dunbar, of Truro, suffered a slight cerebral hæmorrhage while assisting at an operation. Later reports stated that he is progressing favourably.

N. B. DREYER.

Ontario

On October 28th the Annual Clinical Day of the Hamilton Academy of Medicine was held in conjunction with the Hamilton General Hospital. Dr. E. M. Eberts, of Montreal, gave an address on "Surgical Conditions of the Thyroid and Breast"; Dr. F. J. Heck, Assistant Professor of Medicine, Mayo Foundation, Rochester, gave a medical clinic dealing with "Blood Dyscrasias"; and Mr. Louis Blake Duff, Welland, was the guest speaker at the dinner.

The Lincoln County Medical Society held its second Annual Clinical Day in St. Catharines on October 14th. The Medical Clinic was conducted by Dr. Clayton W. Greene, Associate Professor of Medicine, University of Buffalo, Buffalo, N.Y.; while the Surgical Clinic was by Dr. D. E. Robertson, Assistant Professor of Surgery, University of Toronto, Toronto. Dr. Robertson also was the guest speaker at the dinner in the evening. Dr. A. R. MacDonald, President of the Society, acted as Chairman of the meeting.

Dr. F. S. Lawson, who has been in general practice in Warkworth, has recently been appointed to the staff of the Ontario Hospital at Woodstock. Dr. Lawson succeeds Dr. C. V. Tisdale who has been transferred to the Toronto Psychiatric Hospital.

A recent number of the *Ontario Gazette* announced the following appointments:—

Chief Coroners.—Drs. E. T. Kellam, Niagara Falls, for Welland; and Robert MacKinlay, Sarnia, for Lambton County.

Coroners.—Drs. P. M. Brown, Camlachie, for Lambton County; R. B. Gillrie, Mitchell, for Perth County; and W. A. Lewis, Barrie, for Simcoe County.

Dr. W. E. Gallie, Dean of the Faculty of Medicine and Professor of Surgery at the University of Toronto, has been invited to be surgeon-in-chief of the Hospital for the Ruptured and Crippled, New York, for one week, one of the highest tributes a medical man may earn on this continent. When he goes to the hospital, November 2nd, he will be returning to an institution in which he was a house surgeon 30 years ago.

J. H. ELLIOTT.

Saskatchewan

Dr. T. A. Patrick, of Yorkton, was presented with a beautiful desk set by his colleagues as a token of respect for his nearly half century of service, at a meeting of the Northeastern Saskatchewan Medical Association. The presentation was made, following a luncheon in the Yorkton Hotel by Dr. Christie, of Esterhazy, who referred to Dr. Patrick's long and honourable career in the medical profession. The gift consisted of a pen and pencil, a desk lamp, and an elaborate desk mat. On the plaque of the desk set was inscribed: "Dr. T. A. Patrick in appreciation of the high esteem in which he is held by members of the Northeastern Saskatchewan Medical Association.

Dr. J. F. Irving, who has long been associated with Dr. Patrick in Yorkton, spoke briefly of the years of service rendered by Dr. Patrick. "When I first came to Yorkton as a mere youth, I had extended the hand of friendship from Dr. Patrick. I found him ever willing to assist in those difficulties which present themselves to a young doctor, I never met a man whose sincerity and integrity is of such high order as that of our friend whom we honour tonight."

In thanking his colleagues, Dr. Patrick told of his arrival in the Yorkton district nearly a half a century ago. At that time he was the only doctor between Birtle, Manitoba, on the east and Prince Albert on the west, the Qu'Appelle Valley on the south, and the north pole in the north. Through the years which brought other medical men into this district there had been built up a fine spirit among medical practitioners. Never was there a feeling of opposition, but always a fine cooperation. Young doctors had been made welcome, and Dr. Patrick had always left his offices open and his equipment at the disposal of all his colleagues. This spirit of cooperation had made for a better medical service to the sick.

A number of the younger doctors also spoke briefly of the high respect in which they held their "dean". Dr. Patrick had always treated them kindly and was ever willing to assist with his good advice.

Earlier in the day the doctors from this area met at the hospital, where Dr. R. H. MacDonald, of Saskatoon, delivered a paper on "Empyema and Chest Surgery", and Dr. Shepley, of Saskatoon, spoke on "The Early Diagnosis and Treatment of Cancer". Both talks were illustrated with lantern slides.

Dr. Hugh Herbert Christie, Esterhazy, has been appointed representative of the College of Physicians and Surgeons on the Saskatchewan health services Board. He succeeds the late Dr. Vaughan Black, Moose Jaw. Dr. R. O. Davison, Deputy Minister of Health, and Reeve T. W. Hanham, Woodrow, are the other members of the Board. The Secretary, W. G. Sandstrom, is now busy gathering data by mail dealing with the municipal doctor system. Eventually the Board will go into the whole question of state medicine.

Dr. S. E. Moore, of Regina, has been elected president of a newly-formed league which has as its objective the promotion of socialization of medicine in Saskatchewan. The league proposes to gather, tabulate, compile and distribute information from all over the world. Alderman C. L. Dent, of Prince Albert, is Vice-President. The Directors are:—L. J. Waine, Prince Albert; the Rev. W. G. Brown, former Moderator of the United Church, and Frank Eliason, R.F.C., Secretary, Saskatoon; Reeve M. S. Anderson, Bulyea; and J. R. Near, President of the Rural Municipalities Association, Pinkham. The Directors' Board was given power to add two women to its numbers.

LILLIAN A. CHASE.

General

The Association of Officers of the Medical Services of Canada.—The convention dinner of this association was held on October 3rd at the Fort Garry Hotel, Winnipeg.

Thirteen resolutions concerning the internal administration of the Service were dealt with, and papers were read by Lieut.-Col. F. A. Young, Winnipeg, on "The C.C.S. in Practice," and Col. Gorseline, Montreal, on "The Medical Service Under Mechanization".

Mr. J. W. Dafoe, of the *Winnipeg Free Press*, was the guest speaker and based his address on the recent Institute of Pacific Relations' Conference. He outlined the distinguished personnel of the meeting and said that the discussions threw light on many grave problems.

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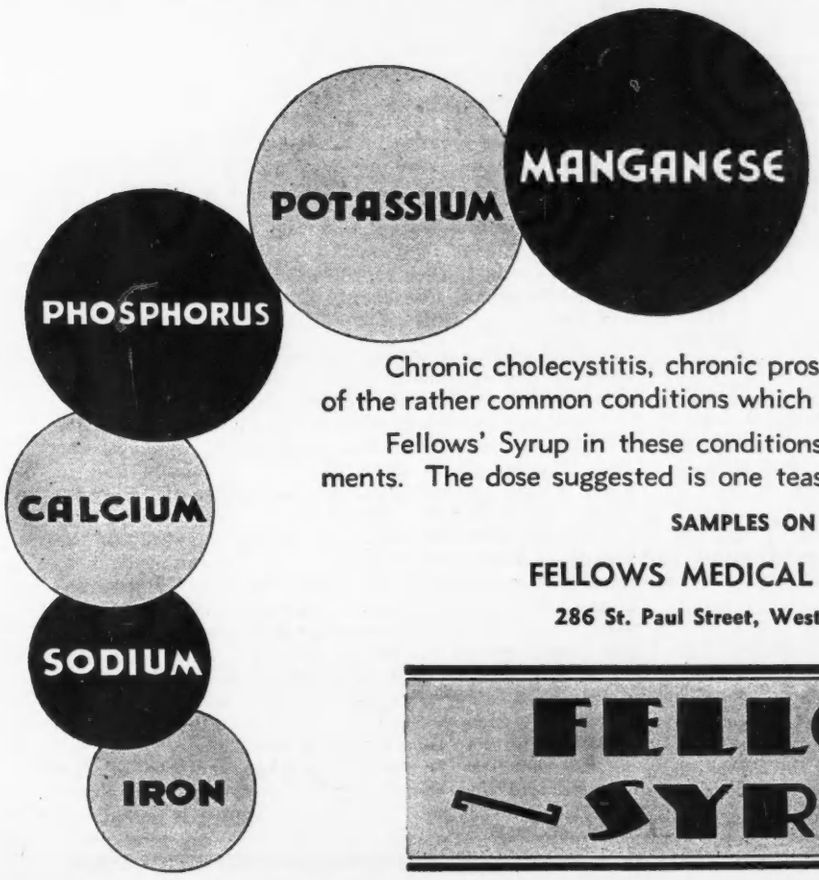

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There was a strenuous effort to keep discussions in the two separate departments—economic and external relations—but they were found to be so intermingled that it was most difficult. It was quite evident that the whole Pacific area, representing a third of the area of the world, represented a district which was "completely rid of the idealism, or folly, if you like to call it, of collective security". Nevertheless the word was on everybody's lips.

Mr. Dafoe spoke of the strong military forces that were active in the world. Russia, under Japanese aggression, was building up a huge army and was today the strongest nation in the League of Nations.

Although the question of collective security seemed dead it might be revived quicker than people thought. The protection of geography was not so sure when the devilish ingenuity of man to take the results of science and devote it to destruction was considered. Mr. Dafoe warned us that "We are taking a long chance if we assume that Canada, one of the most potentially desirable countries, need fear nothing from other countries". He said, in conclusion, that before people threw over the League of Nations they should think of the grave alternative, with countries piling up defences.

Lieut.-Col. W. B. Hendry, Officer Commanding, No. 4 General Hospital, Toronto, was elected *President* of the Association of Officers of the Medical Services of Canada for the coming year. Other officers elected were:—*First Vice-President*—Lieut.-Col. H. Jakes, Regina; *Second Vice-President*—Lieut.-Col. A. Plante, Montreal; *Third Vice-President*—Lieut.-Col. C. Ray, Toronto; *Secretary*—Major F. W. Blakeman, Toronto; *Executive*—Capt. W. W. Barraclough, Toronto; Lieut.-Col. H. D. Courtnay, Ottawa; Col. Shillington, Ottawa; Capt. Houston, Kingston; Major W. A. McKay, Ottawa, and Capt. Athol Gordon, Winnipeg. The treasurer will be elected at a later meeting.

Congress for Medical Post-graduate Development in August 1937.—From the 19th to the 21st of August, 1937, following the invitation of the physicians of the Reich—a congress on medical post-graduate development matters will take place at Berlin with the participation of all German scientific medical societies. Those organizations of foreign countries essentially interested in the matters of medical post-graduate work will also be invited. The foundation of an international committee for the matters of medical post-graduate development will be a special task of the congress.

The congress's manager is the commissioner of the leader of the physicians of the Reich for the service of medical development, Dr. Blome, Berlin.

Office: Kaiserin Friedrich-Haus, Berlin NW 7, Robert-Koch-Platz 7.

The following Canadian medical men, on October 23rd, received Fellowship in the American College of Surgeons:—David M. Archibald, Sydney Mines, N.S.; Rodrique Boisvert, Sherbrooke, Que.; James F. Brunton, Hamilton, Ont.; John A. Tallon, Cornwall, Ont.; Walter B. Carscadden and David W. Pratt, Toronto; Clarence W. Thorne, Melfort, Sask.; Roy L. Anderson and John R. Vant, Edmonton; Lyon H. Applesby and Wilfrid L. Graham, Vancouver.

Two English surgeons, Sir James Walton, of London, and Dr. William Fletcher Shaw, of Manchester, were chosen as Honorary Fellows.

United States

The American Medical Association meets in Atlantic City, N.J., June 7th to 11th, 1937. We are instructed to say that a most cordial welcome to attend this meeting is extended to all members in good standing in the Canadian Medical Association. Upon presentation of membership receipts they will be registered without fee.

Book Reviews

British Encyclopædia of Medical Practice, Including Medicine, Surgery, Obstetrics, Gynæcology and Other Special Subjects. Edited by Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D. Vol. 1, 742 pages, illustrated. Price $10.00 a vol. Butterworth & Co., London, Eng., and Toronto, 1936.

This is an ambitious project and one which bears the marks of the thoroughness and carefulness which one would expect of such an editor and advisory board. Sir Humphry Rolleston opens the first volume with a short introductory essay, in which he sketches the advance of knowledge in medicine, which has been not in a "steady and continuous stream, but at intervals, sometimes of considerable duration". This leads up to a comment on the rapidly shortening lives of medical textbooks and systems, a disadvantage to be overcome in this series by the periodical additions of fresh volumes. Emphasis is laid on the practical aspect of this encyclopædia, and this is greatly aided by the method of alphabetical arrangement of subjects. The writing is clear and condensed; references are given but might be extended in some subjects with advantage.

The series can be thoroughly recommended for the practitioner.

Endocrine Organs in Health and Disease. Sir Humphry Davy Rolleston, Bart., G.C.V.O., K.C.B., M.D., Hon. D.Sc., D.C.L., LL.D. 521 pp.; illustrated. Price $11.00. Oxford University Press, London; McAinsh, Toronto, 1936.

It is extremely difficult to take a comprehensive and succinct view of a subject which has expanded with such enormous rapidity as has endocrinology. The average man is apt to be confused with the prospect of assimilating such a quantity of literature and of keeping abreast of the multiplicity of views and facts. Therefore it is timely that an attempt should be made to put together some account of the growth of our present knowledge. No one is better fitted to do so than Sir Humphry Rolleston, and he gives us here in book form the Fitzpatrick Lectures on the History of the Endocrine Glands. One cannot ask for more compact writing, and the book will be of great and permanent value as a reference volume on an extremely diffuse and rapidly expanding subject.

Pathology of the Nervous System. J. Henry Biggart, M.D., Pathologist to Scottish Asylums' Board. 335 pages; illustrated. Price $4.50. E. & S. Livingstone, Edinburgh; Macmillan Co., Toronto, 1936.

This book has grown out of the lectures given to medical undergraduates and those preparing for the examination for the Diploma of Psychiatry.

Written by a man who has had a wide experience in general pathology, the relationship between the disease processes seen in the nervous tissue and in other tissues of the body is not lost sight of. Because of the increasing specialization of neuropathology and the special technical methods used for the study of the nervous system there is a tendency for the student to regard neuropathology as something entirely separate from general pathology. Intensive study of the nervous system has in recent years greatly advanced the knowledge of the whole subject. This knowledge the author presents in a most understandable form and in its relationship to change in other tissues. The apparent differences are shown to be due to the anatomical factors peculiar to the nervous system.

In the first two chapters the reactions of the neurone and interstitial cells to disease are concisely and clearly explained. The third chapter is concerned

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with the cerebrospinal fluid in disease. The subsequent chapters deal with vascular diseases, acute and chronic bacterial and virus diseases, diseases of unknown etiology, intoxications and deficiency diseases, degenerations, injuries and tumours. A final, short chapter is devoted to errors in development.

The book in no sense is a complete compendium of knowledge of the pathological processes of the nervous system, but it does give a good basic understanding of diseases of that system. To supplement the text a few selected references confined to papers in English are furnished at the end of each chapter. One of the merits of the book is the large number of excellent original illustrations. The undergraduate and, indeed, those practitioners not specializing in neuropathology will find this a most useful book.

The Eye and its Diseases. By Eighty-two International Authorities. Edited by Conrad Berens, M.D., Ophthalmic Surgeon, Pathologist and Director of Research, New York Eye and Ear Infirmary, etc. 1254 pages, illustrated. Price $13.50. W. B. Saunders, London and Phila.; McAinsh, Toronto, 1936.

This is quite an excellent textbook on ophthalmology. It is comprehensive and yet concise, and deals adequately with all phases of the subject. Like many textbooks that have come out in recent years it consists of a series of articles, the authors of which are all men who are distinguished for their attainment in the field on which they write. The articles, therefore, are authoritative. The usual criticism applied to such books is that they lack homogeneity. This is true to a certain extent of this work, though for the most part the unevenesses between article and article have been smoothed out. The book is on the whole excellently illustrated, though a number of the figures, notably those of microscopic sections, are of such low power as to be of little use. The reviewer feels like protesting against a practice which is now found in many medical books of Americanizing the spelling of purely Latin and Greek words, particularly generic terms—for example, Hemophilus. Either Latin, Greek, or American should be used, not a mixture of all. In the last paragraph on page 653 there is a bad typographical error, two or three lines being misplaced. These are about the only criticisms that can fairly be made. On the whole this is an excellent book, and the student of ophthalmology will find himself well repaid in its purchase.

Diseases of the Air and Food Passages of Foreign-Body Origin. Chevalier Jackson, M.D., Sc.D., F.A.C.S., LL.D., Professor of Bronchoscopy and Œsophagoscopy, and Chevalier L. Jackson, A.B., M.D., M.Sc., F.A.C.S., Professor of Clinical Bronchoscopy, Temple University. 635 pages, illustrated. Price $13.75. W. B. Saunders, London and Philadelphia; McAinsh, Toronto, 1936.

This book is unique; nor is there anyone else who would be able to produce such a work. In time to come perhaps some one individual or group will have collected in his or their experience enough clinical material to enable them to speak of thousands of cases such as are here dealt with, but it will be a long time.

The book describes the work of the Jacksons, *père et fils*, in their famous clinic at the Temple University. While it might seem at first that the subject is highly specialized, it will soon be realized that the book contains fruits of experience which are most valuable to all general practitioners. True it is that only a few men take up bronchoscopy, and that even of these few not all will have enough practice of their own to keep their hand in, but it is equally true that every practitioner is vitally interested in it. Sooner or later he will meet with cases either giving a frank history of inhaling foreign objects, or with no such history, but showing all the signs and symptoms of such. In the first instance he will seek the bronchoscopist, whether he has read this book or not. In the second, and possibly more difficult instance, it is quite probable that he will not recognize until too late danger signs which the bronchoscopist, speaking through these pages, would have helped him to interpret aright. The trouble of course is the rarity of cases with foreign objects in the air passages, but the authors do their best to emphasize the need for *always* considering such in diagnosis. The analysis of the factors in the etiology of these foreign objects is extremely interesting. One realizes all through the book that everything in it is founded on actual hard-bought experience. We cannot too strongly recommend the book to internist and specialist alike.

Trachoma. A. F. MacCallan, C.B.E., M.D., F.R.C.S., President of the International Organization against Trachoma. 226 pages, illustrated. Price $7.50. Butterworth & Co. Ltd., London and Toronto, 1936.

The tremendous interest in trachoma, with the resultant intensive research on the subject during the past ten years, particularly since Noguchi's discovery of the *B. granulosus*, makes the appearance of this book very timely. It is very fortunate that such an expert as MacCallan should have taken up the task of sifting and evaluating the data that have been collected. In this book he has done this very completely and impartially. All phases of trachoma are dealt with, from its history, etiology, and diagnosis to its pathology and treatment. In a word, the work is a complete treatise on the subject. It is also excellently written and beautifully illustrated, a majority of the figures being in colour. All in all, this is an outstanding production, well worth its purchase price.

Roentgen Interpretation. A Manual for Students and Practitioners. George W. Holmes, M.D., Professor of Roentgenology, Harvard Medical School, and Howard E. Ruggles, Professor of Roentgenology, University of California Medical School. Fifth edition, 356 pages, illustrated. Price $5.00. Lea & Febiger, Philadelphia, 1936.

The authors in this fifth edition of their book claim as their purpose, "as in the past, to present a brief survey of the field of roentgen-ray diagnosis". For a book of 356 pages it contains a very interesting compilation of concise diagnostic data. As a textbook for students it is full of "meat", but lacks detail for their enlightenment. As a "survey of the field" for the advanced roentgenologist much space has been utilized for data of common knowledge which might well have been used for matters of more recent development. The references given, however, are valuable in supplying this information. The illustrations are equally divided between conditions frequently found and fairly rare cases. It is a volume well worth having as a book of reference, brought up to date by the addition of roentgenological developments in the last five years.

Textbook of Pharmacology and Therapeutics. A. R. Cushny, M.A., M.D., LL.D., F.R.S. Eleventh edition revised by C. W. Edmunds, A.B., M.D., and J. A. Gunn, M.A., M.D., D.Sc., F.R.C.P. 808 pages, illustrated. Price $6.50. Lea & Febiger, Philadelphia, 1936.

This edition brings the book into accord with the eleventh decennial revision of the Pharmacopœia of the United States. Along with some textual revision there has also been re-arrangement of the index. For instance, certain drugs have been grouped together because they act at a common point, *e.g.*, hypnotics, or because of a chemical similarity, *e.g.*, heavy metals. The book maintains its high standard of excellence.